POSTERIOR POLYMORPHOUS CORNEAL DYSTROPHY: A DISEASE CHARACTERIZED BY EPITHELIAL-LIKE ENDOTHELIAL CELLS WHICH INFLUENCE MANAGEMENT AND PROGNOSIS

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INTRODUCTION

POSTERIOR POLYMORPHOUS CORNEAL DYSTROPHY (PPMD) HAS BEEN A SUBJECT OF increasing interest in the past 20 years. There are many pathologic reports of PPMD with clinical summaries of the patients from whom the corneal buttons were removed. However, until now, no large clinical series has been reported discussing keratoplasty to PPMD and the clinical and pathologic factors that influence it. In 1974, Grayson[1] published an excellent review of the condition and stressed its association with iris and anterior chamber changes.

During the past 10 years, I have examined approximately 120 patients with PPMD and performed surgery on 13 of them. I have also had the opportunity to work closely with a number of investigators conducting both clinical and laboratory studies.

The outstanding pathologic finding in posterior polymorphous dystrophy was epithelial-like endothelial cells which, because of their presence and extent, produce a wide spectrum of clinical presentations. The prognosis of surgical procedures to improve vision and lower intraocular pressure is directly related to the pathologic endothelium.

Specifically, this thesis summarizes the results of our laboratory studies and reports for the first time the outcome of corneal and glaucoma surgery for posterior polymorphous dystrophy. It will be the first clinical report of a large series of patients (13) with posterior polymorphous dystrophy who underwent penetrating keratoplasty. Several clinical and laboratory factors influenced the prognosis.

TR. AM. OPHTH. SOC. vol. LXXXIII, 1985

The clinical and laboratory sections will be presented in the order of our experience. We first examined and started operating on patients with PPMD. We then began laboratory investigations, the results of which have influenced our further clinical management. Thus, the order was clinical, then laboratory, then clinical.

HISTORICAL REVIEW

A comprehensive historical review of posterior polymorphous dystrophy was published by Grayson[1] in 1974. Milestones in the clinical characterization of posterior polymorphous dystrophy began with the first published description of the condition by Koeppe[2] in 1916. He reported "bullous" lesions on the posterior corneal surface in six patients. Iris adhesions to the cornea, which are now a well-recognized potential finding in PPMD, were reported by Soukup[3] in 1964. Glaucoma is not an uncommon feature of posterior polymorphous dystrophy. The association of glaucoma and PPMD was pointed out in 1968 by Rubenstein and Silverman.[4]

Although previous reports have stated that posterior polymorphous dystrophy might rarely be inherited as an autosomal recessive inheritance condition,[5] it is basically an autosomal dominant disease. The autosomal dominant transmission was reported in 1953 by McGee and Falls.[6]

The histopathologic investigation of PPMD began in 1967 by Morgan and Patterson.[7] Using light microscopy, they reported irregular thickenings of Descemet's membrane and protrusions of the thickened Descemet's membrane into the anterior chamber. In 1971, Boruchoff and Kuwabara[8] published electron microscopic findings in posterior polymorphous dystrophy. They stressed the important feature of epithelial-like endothelial cells.

In 1974, Grayson[1] summarized the clinical and pathologic features of PPMD. He characterized the condition both clinically and pathologically in great detail, stressing the importance of associated anterior chamber changes.

During the past decade there has been an acceleration of both clinical and histologic studies of posterior polymorphous dystrophy. This thesis will describe the results of these studies performed both at our institution and by others giving the results of medical and surgical management of posterior polymorphous dystrophy in a large number of patients.

MATERIALS AND METHODS

CLINICAL

I have examined about 120 patients with posterior polymorphous dystrophy of the cornea during the past 10 years. In general, patients coming to keratoplasty had either moderate or severe corneal pathology. Moderate cases were those with diffuse stromal and epithelial edema and either scattered islands of posterior pathology or diffusely involved endothelial and Descemet's layers. Severe cases had anterior scarring and often degenerative (calcific and lipid) changes that obscured the view of the posterior cornea. This definition of "moderate" and "severe" will be used in Table I and in discussing the results of keratoplasty.

What follows is a compilation of case reports of 13 consecutive patients from six families on whom I performed 22 corneal transplants (Table I). This series is evaluated in an attempt to draw some conclusions on the clinical course and prognosis of penetrating keratoplasty for posterior polymorphous dystrophy. Figures of families 1 through 4 are modifications of illustrations from a previous report.[5]

CASE REPORTS

CASE I (FAMILY 1, V-3)

We first examined this 22-year-old white woman on September 25, 1974, when she was 11 years old (Fig 1). She complained of slow, painless, decreasing vision in both eyes (OU) for the previous 6 years, with marked worsening of vision of the last several months. Cloudy corneas were first noted at the age of 4 years.

She had a visual acuity of 20/200 OU at the time of the examination. Both corneas revealed severe disease, including moderate microcystic edema of the epithelium, diffuse stromal edema, and calcific degeneration (Fig 2). There were many vesicle-like lesions at the level of a thickened Descemet's membrane. Intraocular pressure was 18 mm Hg in the right eye (OD) and 16 mm Hg in the left eye (OS). No iridocorneal adhesions could be seen through the cloudy cornea. Posterior segment examination was unremarkable. Her father had a very mild case of PPMD, which included typical band-like lesions and thickened Descemet's membranes (Fig 3). One month later she underwent a 7.5 mm penetrating keratoplasty OD under general anesthesia without complications. The postoperative course was unremarkable and there were no elevations of intraocular pressure and no episodes of graft rejection. In November 1975, she underwent a 7.5 mm penetrating keratoplasty OS under general anesthesia without complications. Again the postoperative course was unremarkable without problems of elevated intraocular pressure or graft rejection. Her best-corrected visual acuity 7 years later was 20/30 OU (Fig 4).

TABLE I: SUMMARY OF PRE- AND POSTOPERATIVE DATA ON 22 CORNEAL TRANSPLANTS FOR POSTERIOR POLYMORPHOUS DYSTROPHY

CASE NO	EYE	AGE* (YRS)	PREOP VISUAL ACUITY	MODERATE (M) OR SEVERE (S) CORNEAL DISEASE†	BROAD-BASED IRIDOCORNEAL ADHESIONS‡	PREOP ELEVATED IOP§	POSTOP ELEVATED IOP§	POSTOP VISUAL ACUITY‖	CLEAR TRANSPLANT	REASON FOR FAILURE	ENDOTHELIAL REJECTION REACTION	RETROCORNEAL MEMBRANE
1	OD	11	20/200	S	No	No	No	20/30	Yes		No	No
1	OS	12	20/200	S	No	No	No	20/30	Yes		No	No
2	OS	39	20/400	M	No	No	No	20/40	Yes		No	No
3	OD	74	LP¶	S	Yes	Yes	Yes	20/400	Yes		No	Yes
4	OS	59	CF#	M††	Yes	Yes	Yes	NLP	No	G1‖‖	No	No
5	OS	25	HM**	M††	Yes	Yes	Yes	HM	No	Rejection	Yes	No
5	OS	27	HM	M	Yes	Yes	Yes	HM	No	RCM¶¶/G1	No	Yes
6	OD	70	CF	M	Yes	Yes	Yes	LP	No	G1	Yes	No
6	OD	77	LP	M	Yes	Yes	Yes	CF	No	RCM	No	Yes
7	OS	28	20/200	M	No	No	No	20/40	Yes		NO	No
7	OD	31	20/80	M	No	No	No	20/200	No	Rejection	Yes	No
8	OD	53	HM	S	Yes	Yes	Yes	HM	No	G1/Rejection	Yes	No
8	OS	56	20/400	S	Yes	Yes	Yes	20/30	Yes		No	No
9	OD	55	CF	S	Yes	Yes	Yes	20/400	No	G1	No	No
9	OS	58	LP	S	Yes	Yes	Yes	20/400	No	RCM/G1	No	Yes
10	OD	37	CF	M	Yes	Yes	Yes	20/40	Yes		Yes	No
11	OD	50	CF	S	No	No	No	20/80§§	Yes		No	No
11	OS	51	20/400	S	No	No	No	20/40§§	Yes		Yes	No
12	OS	57	20/300	M	Yes‡‡	Yes	Yes	20/25	Yes		No	No
12	OD	58	20/100	M	Yes‡‡	Yes	Yes	20/25	Yes		No	No
13	OD	43	20/80	M	No	No	No	20/30	Yes		No	No
13	OS	44	20/70	M	No	No	No	20/20	Yes		Yes	No

*Age at time of each corneal transplant.
†At time of first corneal transplant. Refer to introductory section of Materials and Methods, Clinical.
‡Seen grossly by slit lamp examination unless otherwise indicated.
§Intraocular pressure elevated above 20 mm Hg.
‖Best-corrected visual acuity at last visit. Follow-up ranged from 13 months to 9 years except for the second transplant on case 6 (4 months).
¶Light perception.
#Counting fingers.
**Hand motions.
††Evaluation from records, not personal examination.
‡‡Adhesions seen only on gonioscopy.
§§Nuclear sclerotic cataract.
‖‖Glaucoma.
¶¶Retrocorneal membrane.

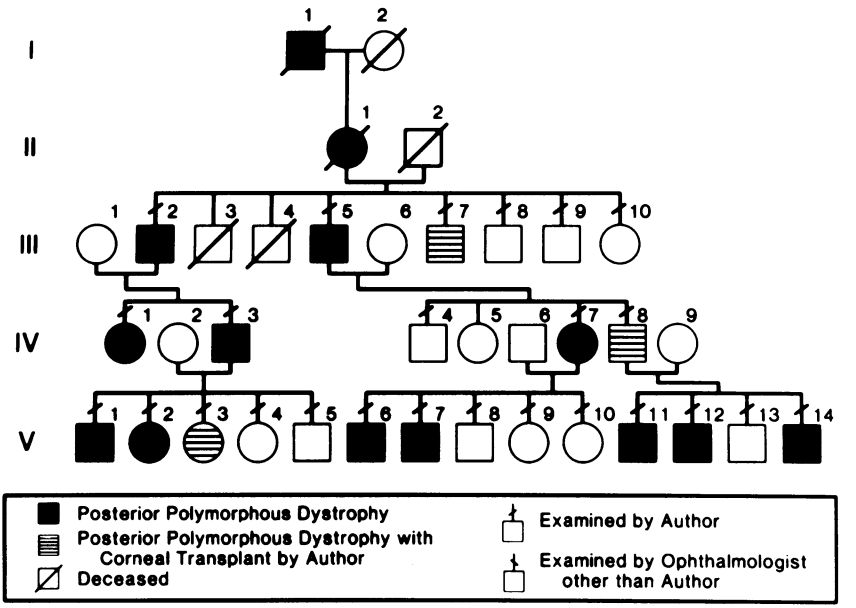

FIGURE 1
Pedigree of Family 1.

CASE 2 (FAMILY 1, IV-8)

This 48-year-old white man was first seen by us on August 29, 1975, at the age of 39 years. He gave a history of painless decreasing visual acuity more pronounced in the left eye over the last 10 years. Visual acuity was 20/60 OD and 20/400 OS. His corneas revealed moderate disease. There was epithelial and stromal edema which was worse in the left eye. Descemet's membrane was diffusely thickened (Fig 5). No iridocorneal adhesions were noted. Intraocular pressure measured with a McKay-Marg tonometer was 14 mm Hg OD and 15 mm Hg OS. Posterior segment examination was unremarkable. One month later the patient underwent an 8 mm penetrating keratoplasty OS under local anesthesia without complications. His postoperative course was unremarkable without elevation of intraocular pressure or episodes of graft rejection. Best-corrected visual acuity at a 2 year follow-up was 20/40.

CASE 3 (FAMILY 1, III-7)

This 84-year-old white man was first seen by us on August 25, 1975, when he was 74 years old complaining of poor vision OU for many years. He gave a history of a cataract extraction on the left eye 2 years previously and bilateral filtering operations for glaucoma several years before. He had required acetazolamide for con-

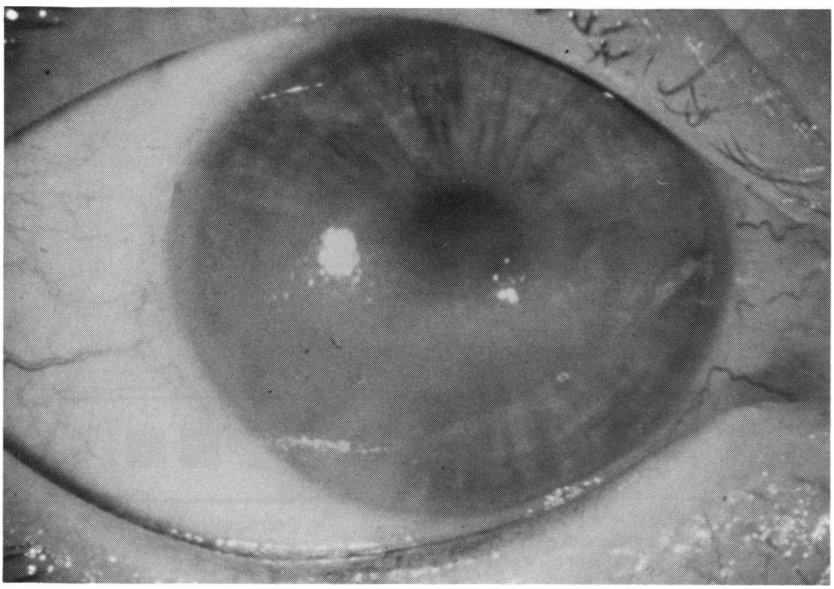

FIGURE 2
Case 1 (Family 1, V-3). Preoperative slit lamp photo OD showing diffuse corneal edema and band keratopathy in an 11-year-old with posterior polymorphous dystrophy.

trol of his intraocular pressure for many years. On examination the visual acuity was light perception, with projection inferiorly and temporally OD and light perception with poor projection OS. The right cornea had severe disease which included marked epithelial microcystic edema as well as diffuse stromal edema and scarring (Fig 6). The endothelial surface could not be visualized. There were iris adhesions to the posterior corneal surface for approximately 180°. The left cornea had similar microcystic and stromal edema with iris adhesions. Intraocular pressure measured with a McKay-Marg tonometer was 22 mm Hg OD and 32 mm Hg OS. The fundi could not be seen; however, echographic examination revealed no abnormalities of the posterior segment. On September 5, 1975, the patient underwent an 8 mm penetrating keratoplasty and intracapsular cataract extraction OD under local anesthesia. The procedure was complicated by the vitreous face presenting in the wound necessitating a pars plana vitreous aspiration. Postoperatively, the graft remained clear centrally. A retrocorneal membrane was noted inferiorly 3 weeks after surgery which did not progress. Intraocular pressure was controlled at approximately 20 mm Hg with pilocarpine, timolol, and acetazolamide. Unfortunately, the right optic nerve was atrophic with a cup-to-disc ratio of 0.9. Visual acuity 2 years postoperatively was 20/400.

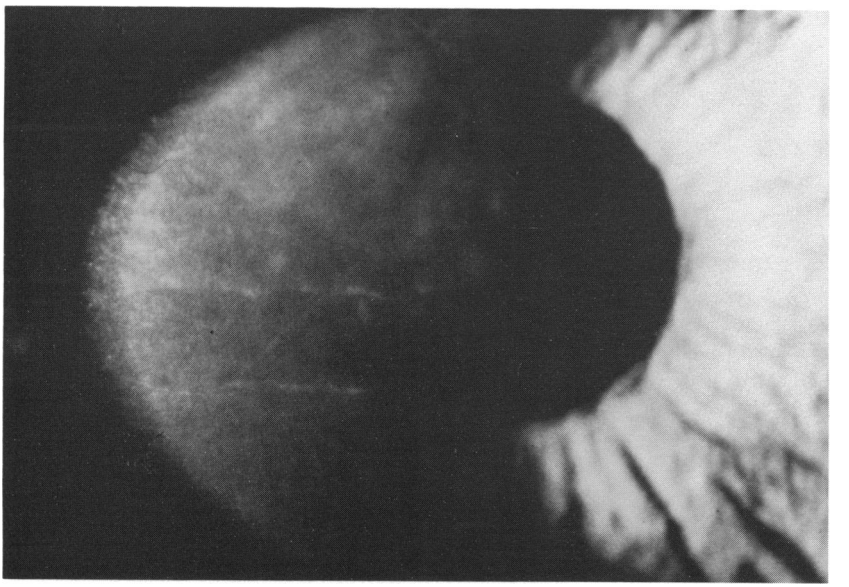

FIGURE 3
Forty-eight-year-old father (Family 1, IV-3) of case 1. Band-like posterior corneal lesion and diffuse thickening of Descemet's membrane demonstrating less extreme PPMD than his daughter.

CASE 4 (FAMILY 2, III-5)

This 68-year-old white woman had been previously seen at our institution beginning in June 1966, at the age of 50 years (Fig 7). At that time, she had posterior vesicular lesions and broad-based iridocorneal adhesions OU. Intraocular pressure was 16 mm Hg OU. In June 1974, under local anesthesia she underwent an 8 mm penetrating keratoplasty OS at another hospital. There were no intraoperative complications. The postoperative course was complicated by an elevated pressure requiring pilocarpine, epinephrine, and acetazolamide.

I first examined the patient in September 1974. Her visual acuity was 20/50 OD and 20/200 OS. Intraocular pressure were 15 mm Hg OU. She had an edematous, failed corneal transplant OS. The right cornea demonstrated moderate disease. She had diffuse but mild epithelial edema, moderate stromal edema, extensive thickening of Descemet's membrane, and irregularity of the posterior corneal surface. A glass-like membrane extended from the back of the cornea onto the iris. The iris was adherent to the cornea at these sites (Fig 8). In March 1975, her visual acuity deteriorated to counting fingers OS. The patient underwent a repeat penetrating keratoplasty OS under local anesthesia. There were no intraoperative complications. Postoperatively, there were again problems with elevated intraocular pressure, with the pressure ranging from 25 to 36 mm Hg while using

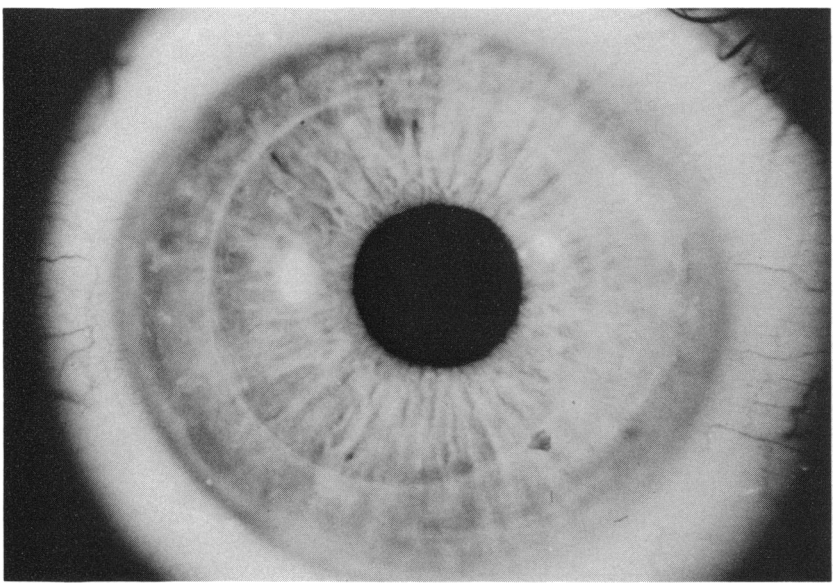

FIGURE 4
Case 1 (Family 1, V-3). Two years after penetrating keratoplasty OD. Visual acuity 20/30.

acetazolamide, epinephrine, and pilocarpine. By January 1976, a dense cataract had formed in the left eye and an extracapsular cataract extraction was performed. The elevation of the intraocular pressure continued, reaching 50 mm Hg while using acetazolamide, epinephrine, and pilocarpine. In 1979, because she had a large afferent pupillary defect, we decided not to do further surgery on her left eye. The graft slowly became opaque. In August 1981, the patient was using timolol, epinephrine, and pilocarpine. Visual acuity was 20/100 OD and no light perception OS. She had a large afferent pupillary defect OS. Intraocular pressure in the left eye was 22 mm Hg and the graft was totally opaque.

CASE 5 (FAMILY 2, IV-21)

This 35-year-old white man was first seen by us in January 1975, at the age of 25 years with a history of a failed corneal transplant OS in 1963 at another hospital for a corneal dystrophy. His first examination at our institution was in 1958 at the age of 9 years. At that time he had marked posterior corneal changes and a "pupillary membrane remnant extending into the anterior chamber" on the right. On examination in January 1975, his visual acuity was 20/40 OD and hand movements OS. The right eye revealed no epithelial edema but very slight stromal edema. Descemet's membrane was irregular, rough and thickened. There were multiple plaques of extreme posterior thickening (Fig 9). Several areas of iridocorneal

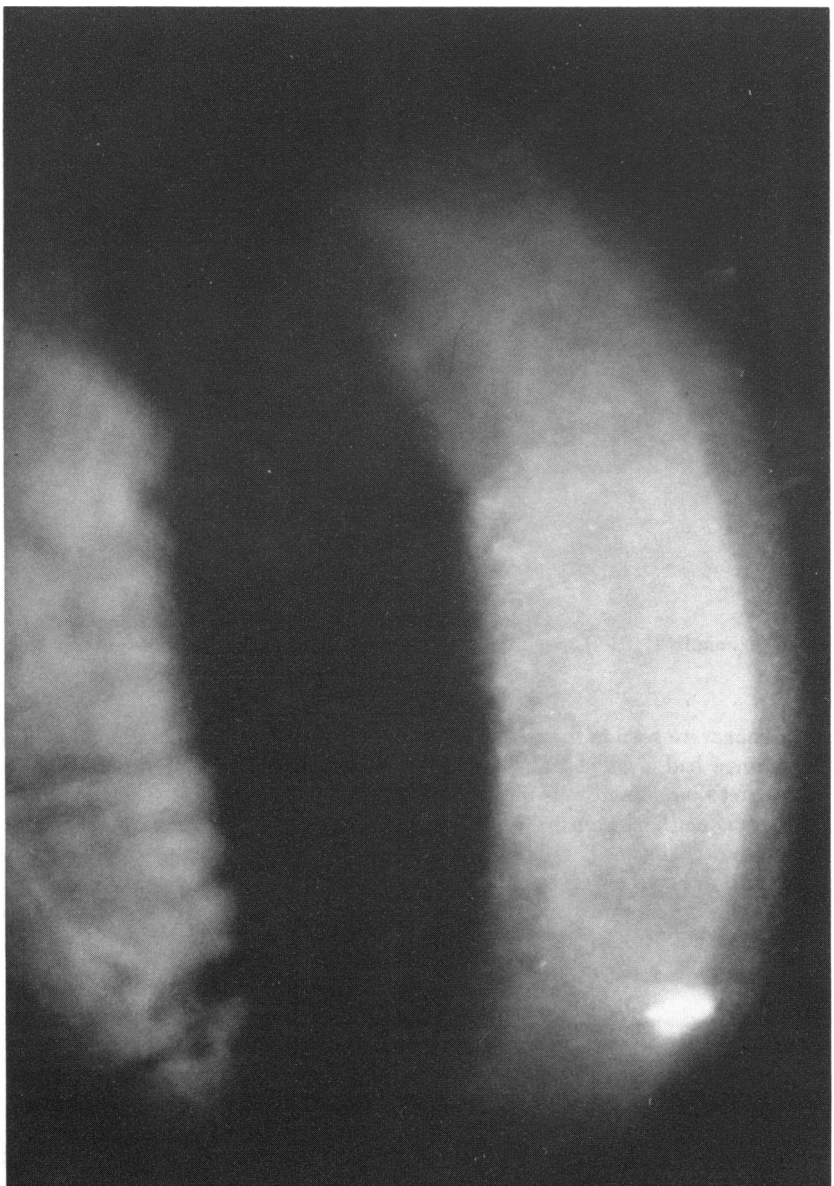

FIGURE 5
Case 2 (Family 1, IV-8). Thirty-nine-year-old male with PPMD demonstrating diffuse corneal edema and thickening of Descemet's membrane OS.

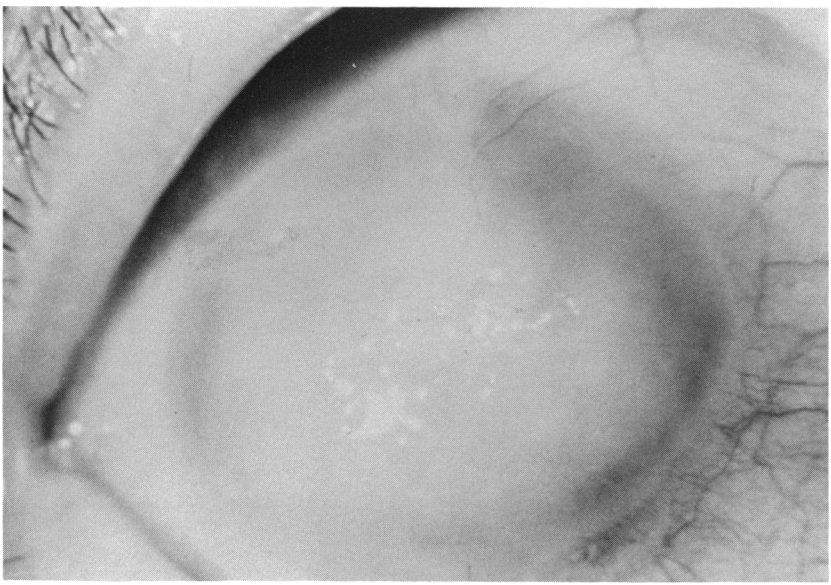

FIGURE 6
Case 3 (Family 1, III-7). Severe corneal scarring from PPMD. Preoperative photo of 74-year-old male patient.

adhesions were seen in the periphery of the cornea by slit lamp examination. The left cornea had a failed transplant with marked epithelial and stromal edema. Descemet's membrane was markedly thickened peripheral to the donor button. There was neither extensive scarring peripheral to the failed transplant nor degenerative changes. Therefore, the extent of corneal disease was defined as moderate rather than severe. Iridocorneal adhesions were present. Intraocular pressures were 24 mm Hg OU. He had three daughters, two of whom also have the dystrophy (Figs 10 and 11).

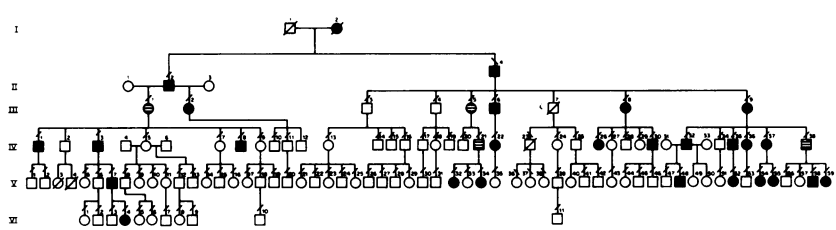

FIGURE 7
Pedigree of Family 2 (see Fig 1 for key).

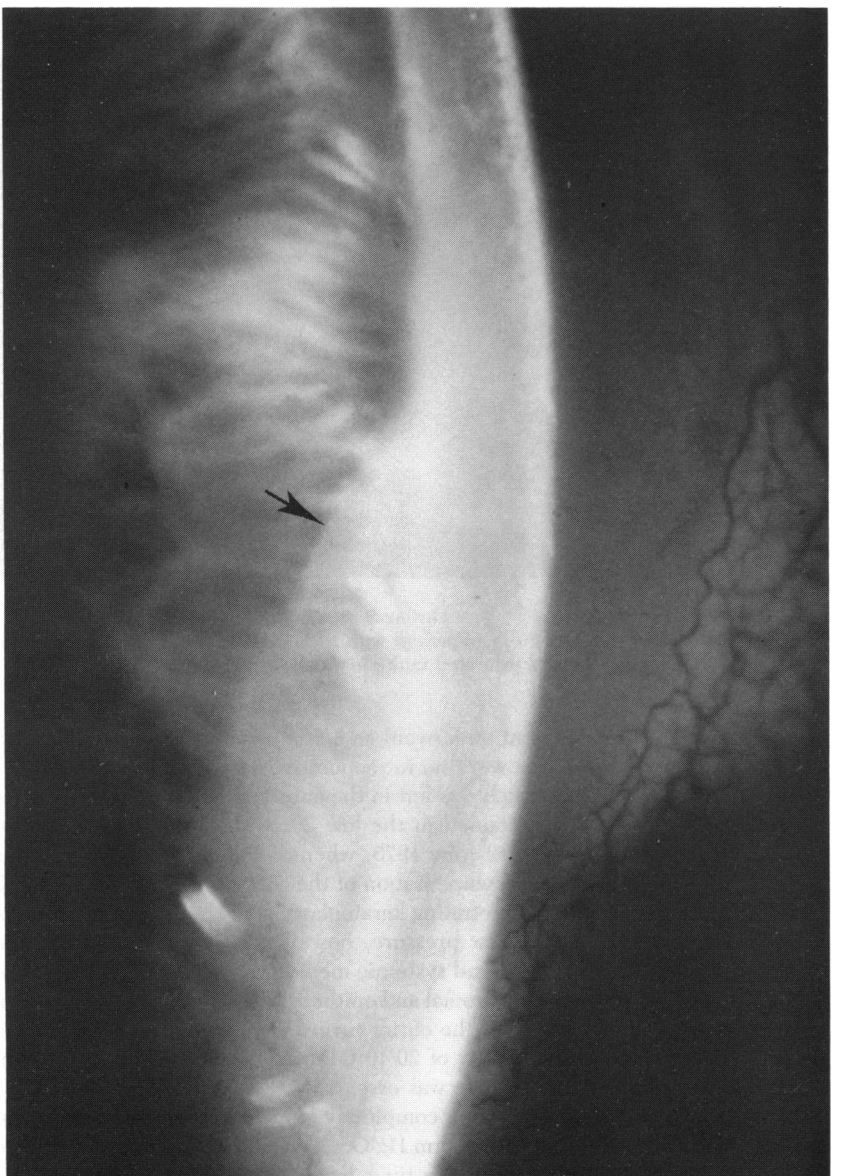

FIGURE 8
Case 4 (Family 2, III-5). Fifty-eight-year-old white female with PPMD. Right eye demonstrates corneal edema, thickened Descemet's membrane, and a glass-like membrane from posterior cornea to iris and iridocorneal adhesion (*arrow*).

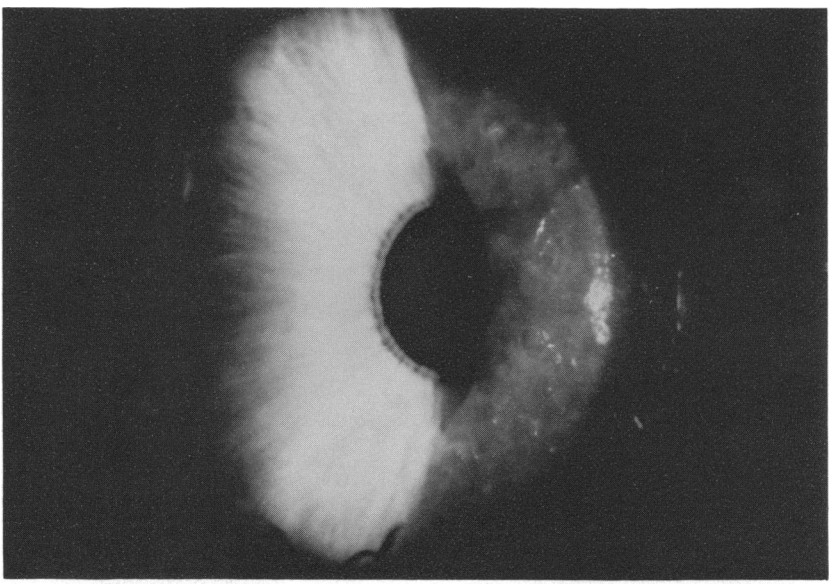

FIGURE 9
Case 5 (Family 2, IV-21). Right eye of patient with PPMD. Posterior corneal surface was diffusely irregular and exhibited multiple areas of extreme thickening.

In February 1975 the patient underwent an 8 mm penetrating keratoplasty OS under local anesthesia. There were no intraoperative complications except for a moderate amount of blood which was left in the anterior chamber. Postoperative intraocular pressure was maintained in the low 20s with the help of acetazolamide. The patient did well until June 1975, when an endothelial graft rejection developed. This resulted in decompensation of the corneal transplant. In March 1976 he underwent a repeat penetrating keratoplasty OS. There were no intraoperative complications. Intraocular pressure, however, was in the mid 30s and could not be lowered by topical and systemic medication. The corneal transplant gradually developed increasing stromal and epithelial edema. In addition, a retrocorneal membrane formed across the entire cornea. The patient was last seen in February 1983 with a visual acuity of 20/40 OD and hand movements OS. Slit lamp evaluation of the right cornea was essentially the same as that recorded 8 years previously. The left eye had a completely failed corneal graft. Intraocular pressure was 15 mm Hg OD and 30 mm Hg OS. The patient was comfortable and no further treatment is planned at this time.

CASE 6 (FAMILY 2, III-1)

This 74-year-old white woman was first seen by us in April 1974, at the age of 67 years. She presented with a history of gradually decreasing vision OD for several

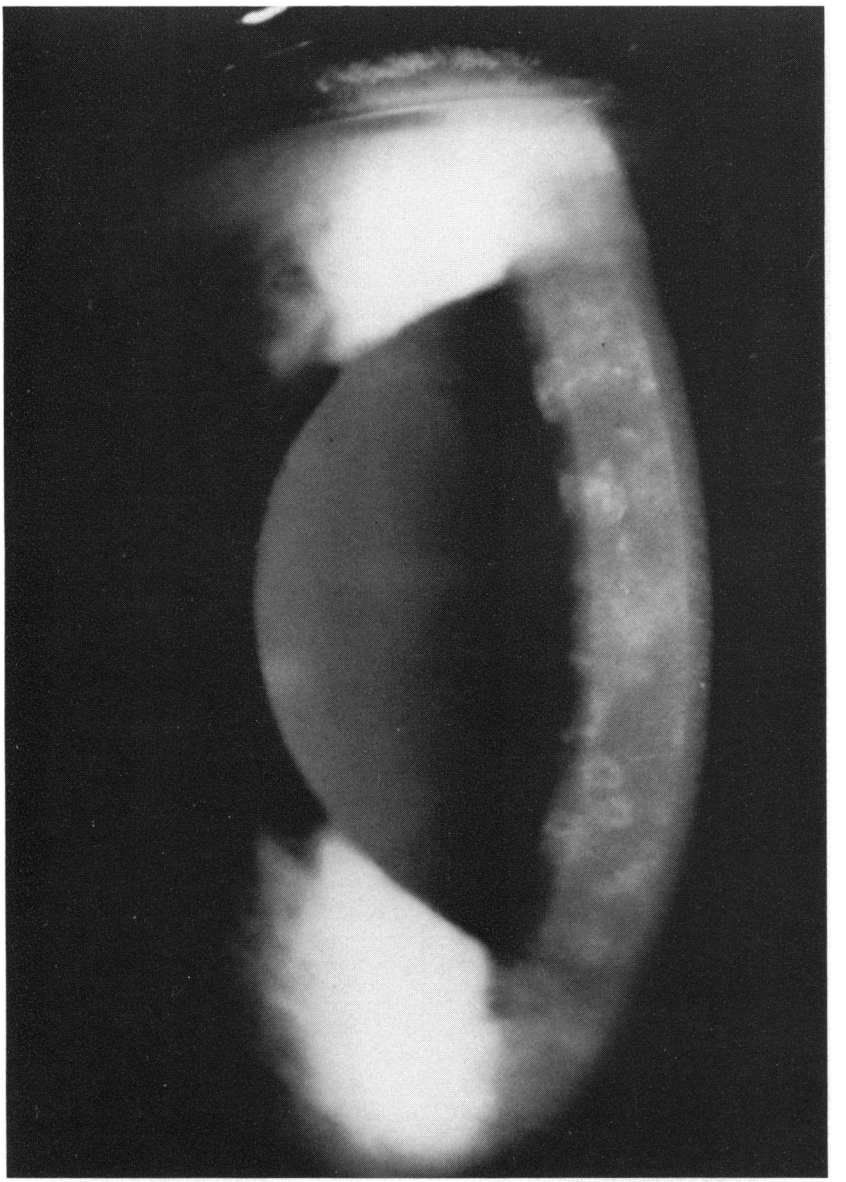

FIGURE 10
Ten-year-old daughter (Family 2, V-34) of case 5. PPMD of right eye showing posterior lesions which appear more discrete than those of her father because of relatively clear cornea anterior to them.

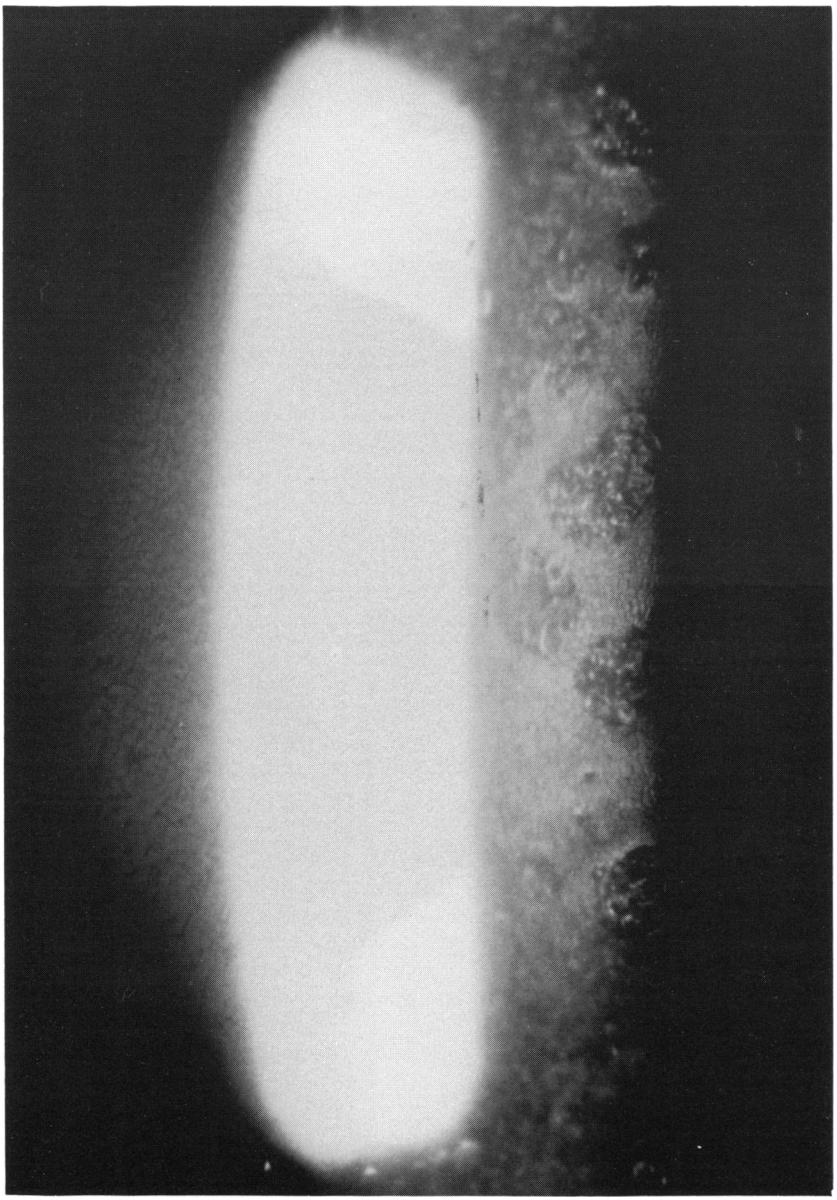

FIGURE 11
Twelve-year-old daughter (Family 2, V-32) of case 5. Specular microscopy OS reveals islands of abnormal cells between a relatively normal-appearing endothelial mosaic.

years. She was being treated for glaucoma OU. Visual acuity was counting fingers OD and 20/40 OS. The right cornea demonstrated moderate corneal disease. Slit lamp examination disclosed moderate epithelial and stromal edema and areas of Descemet's membrane which were thickened with classic vesicle-like formation scattered throughout. There was pupillary ectropion with a glass-like membrane extending from the posterior cornea across the temporal chamber angle, onto broad iridocorneal adhesions temporally (Fig 12), and over to pupillary uveal ectropion. The left eye did not have epithelial edema but did have minimal stromal edema. Descemet's membrane was thickened and there were vesicles at this layer in the periphery of the cornea. Intraocular pressure was 29 mm Hg OD and 24 mm Hg OS on maximum medical therapy. In February 1975 the patient underwent a trabeculectomy and cataract extraction OD under local anesthesia. Postoperatively she required acetazolamide and pilocarpine. Intraocular pressure remained in the mid 20s and the epithelial edema increased.

In October 1977, when the visual acuity was counting fingers at three feet, the patient underwent a 9 mm penetrating keratoplasty OD under local anesthesia. There were no intraoperative complications. The postoperative course was complicated by persistently elevated intraocular pressure while using acetazolamide, pilocarpine, and epinephrine. In January 1978 the patient showed signs of an endothelial graft rejection characterized by an endothelial rejection line, many keratic precipitates, and moderate anterior chamber reaction. The graft rejection cleared with topical steroid treatment. Because of the persistently elevated intraocular pressure, in August 1978, the patient underwent cyclocryotherapy of the inferior ciliary body with six applications of −80°C freezing for 60 seconds. At this time it was noted that there was glaucomatous cupping and atrophy of the optic nerve on the right. The transplant gradually decompensated.

Because of the development of painful bullous keratopathy OD and a chance for some visual improvement, the patient underwent a repeat penetrating keratoplasty of 10 mm under local anesthesia on August 31, 1984. There were no intraoperative complications. Postoperatively, the intraocular pressure was 12 mm Hg and the graft was initially clear. However, 1 month later, it was noted that a membrane was beginning to grow across the posterior surface of the cornea (Fig 13). It was postulated that this represented either a form of epithelial downgrowth or possibly a recurrence of the posterior polymorphous dystrophy. Visual acuity was counting fingers at one foot OD and 20/100 OS. The decrease in vision in the left eye was thought secondary to cataractous changes rather than further corneal decompensation. Intraocular pressure was 10 mm Hg OD and 22 mm Hg OS. Laboratory examination of the corneal button removed at the time of her second transplant revealed typical epithelial-like cells growing across the posterior surface of the cornea. This finding will be the subject of a future report.

CASE 7 (FAMILY 2, IV-38)

This 39-year-old white man was first seen at our institution on August 2, 1973, when he was 26 years old. He gave a history of marked photophobia and gradually

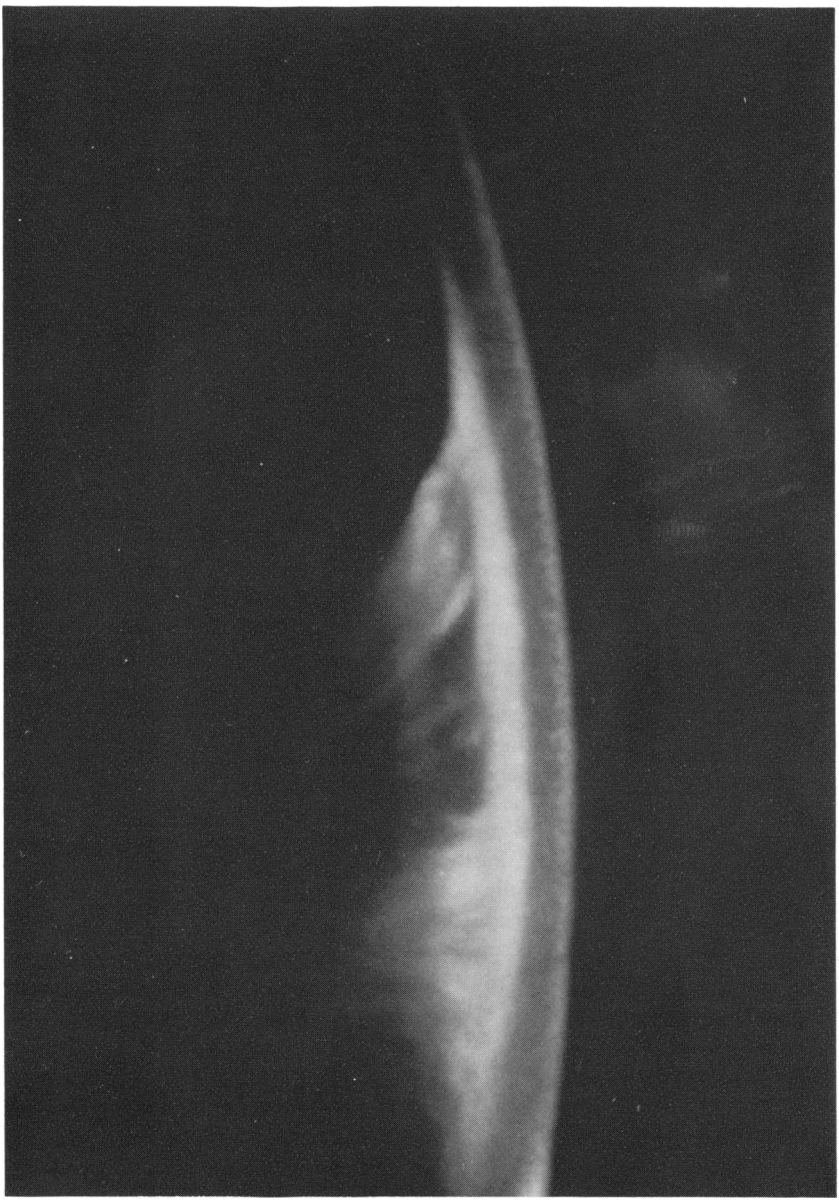

FIGURE 12
Case 6 (Family 2, III-1). Seventy-year-old white female with broad-based iridocorneal adhesion and thickened Descemet's membrane preoperatively OD.

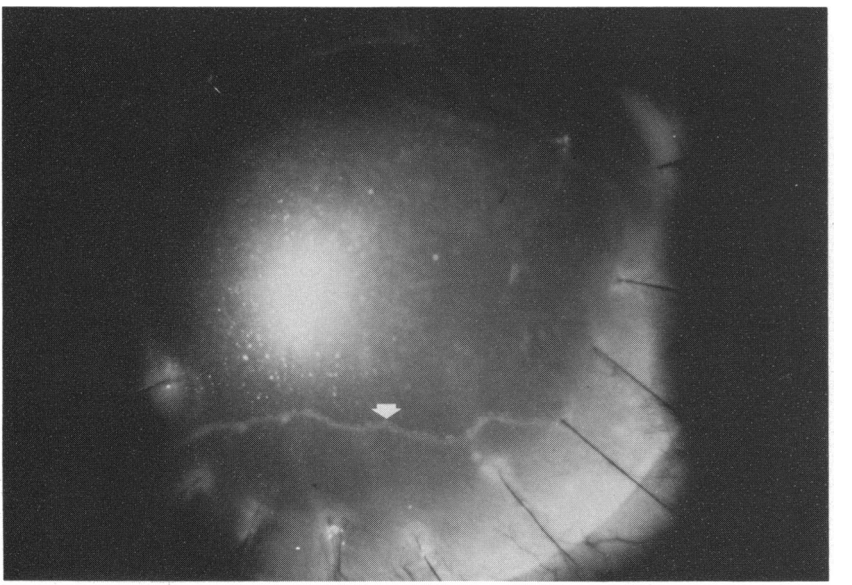

FIGURE 13
Case 6 (Family 2, III-1). One month postoperatively for second corneal transplant OD, a retrocorneal membrane was growing up from the inferior wound (*arrow at edge of membrane*).

decreasing intraocular OU. Visual acuity was 20/30 OU. Both corneas had moderate disease with diffuse polymorphous opacities of the posterior cornea. There was no epithelial or stromal edema. Intraocular pressure was 16 mm Hg OD and 14 mm Hg OS. Gonioscopic examination revealed no iridocorneal adhesions. In the subsequent 8 months the patient noticed decreased intraocular pressure OS.

I first examined him in April 1974. He had developed bullous keratopathy. His visual acuity was 20/200. On June 2, 1974, he underwent an 8 mm penetrating keratoplasty OS under general anesthesia because he would not agree to local anesthesia. There were no intraoperative complications. Postoperatively the patient did well without elevated intraocular pressure or episodes of graft rejection. By July 1977, his right eye had developed moderate epithelial and stromal edema and the visual acuity had decreased to 20/80 (Fig 14). On July 18, 1977, the patient underwent an 8 mm penetrating keratoplasty OD under local anesthesia. There were no intraoperative complications. Postoperatively the intraocular pressure was well controlled without medication. On October 4, 1978, subepithelial infiltrates and a moderate anterior chamber reaction were seen in the right eye. This rejection episode was treated with intensive topical corticosteroid drops and resolved. In October 1979, the patient was doing well with a visual acuity of 20/30

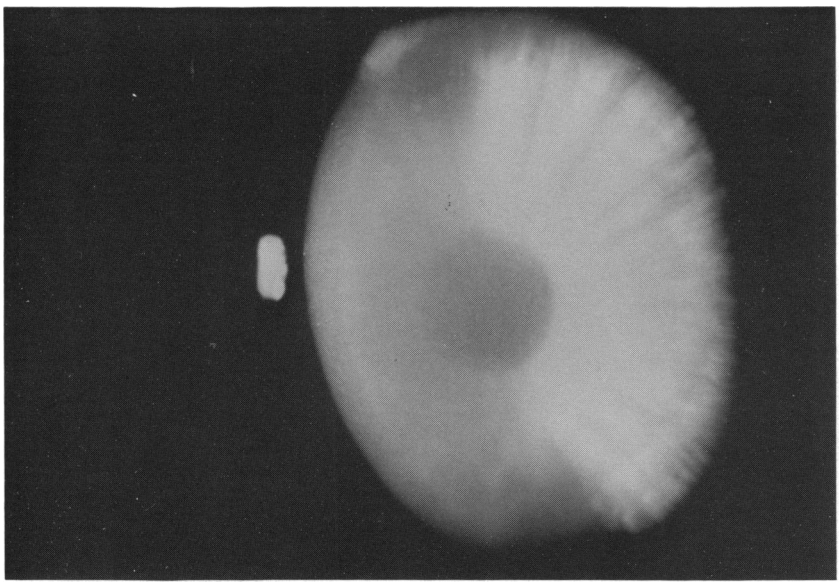

FIGURE 14
Case 7 (Family 2, IV-38). Preoperative photo of 28-year-old white male with PPMD demonstrating an evenly diffuse stromal and epithelial edema.

OU. His 7-year-old daughter (Fig 15) and 9-year-old son (Fig 16) showed classic PPMD changes on specular microscopy.

In February 1980, the patient had another episode of graft rejection OD, characterized by diffuse subepithelial infiltrates, keratic precipitates, and moderate anterior chamber reaction. This was treated with intensive topical corticosteroids. The patient missed many return appointments. We had reason to question his compliance to our therapy. Unfortunately the graft rejection became a chronic problem in his right eye and visual acuity at the last follow-up on August 19, 1980, had decreased to 20/200 OD and 20/40 OS. He refuses to return for further examination.

CASE 8 (FAMILY 3, II-1)

I first examined this 59-year-old white man in 1975 when he was 49 years old (Fig 17). I did not take over his care, however, and perform surgery until June and July of 1979. He was first seen at our institution in 1947 at the age of 22 years. At that time his visual acuity was 6/200 OD and 9/200 OS. He had epithelial and stromal edema OU and band keratopathy OS. The diagnosis was Fuchs' dystrophy. In 1948 he underwent a penetrating keratoplasty OD at another institution. The operation failed and he was next seen in our department in October 1972. At that

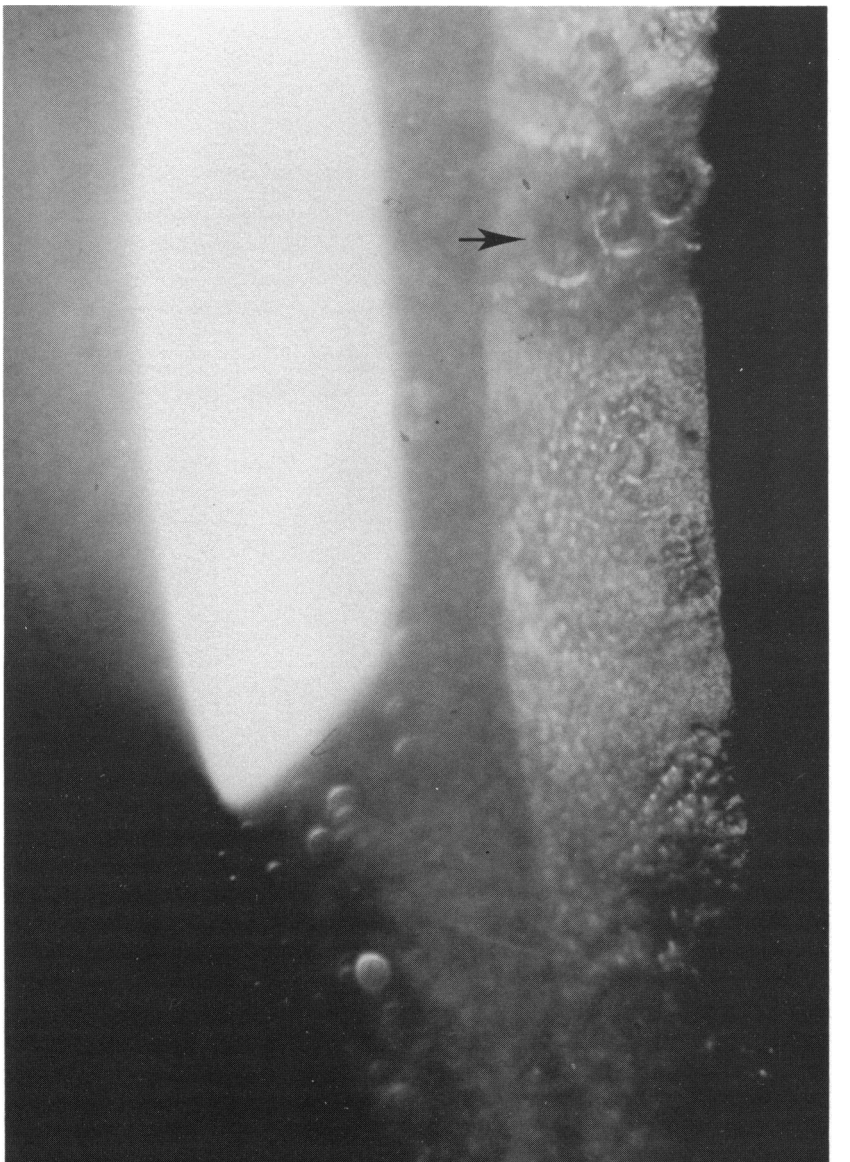

FIGURE 15
Seven-year-old daughter (Family 2, V-59) of case 7. Specular photomicrograph revealing vesicular-like (*arrow*) and other islands of abnormal cells in a normal-appearing endothelial mosaic.

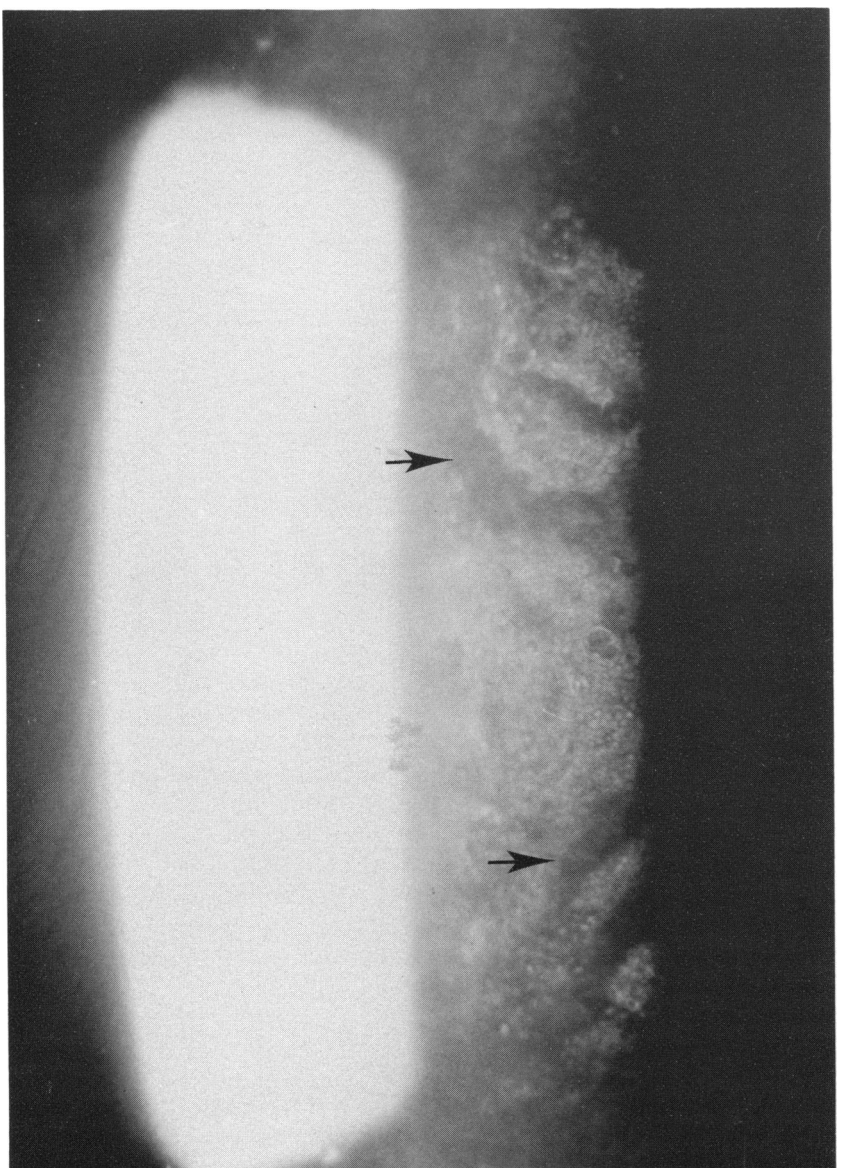

FIGURE 16
Nine-year-old son (Family 2, V-58) of case 7. Specular photomicrograph reveals wavy areas of an abnormal posterior surface (*arrows*) between a normal-appearing endothelial mosaic.

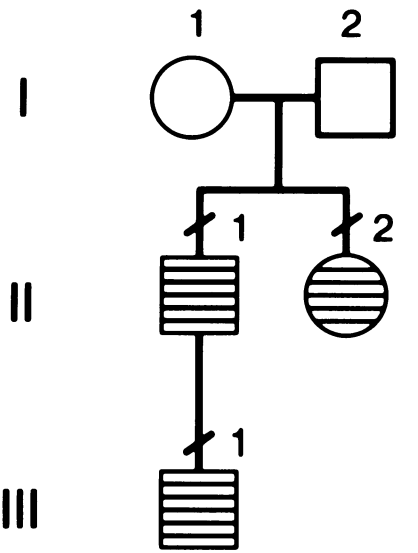

FIGURE 17
Pedigree of Family 3 (see Fig 1 for key).

time his visual acuity was counting fingers at one foot OD and light perception with good projection OS. Both corneas showed extensive scarring. Intraocular pressures were 32 mm Hg OD and 28 mm Hg OS. On November 20, 1972, he underwent another penetrating keratoplasty OD. Postoperatively, there were problems with elevated intraocular pressure and graft rejection.

During his postoperative course, along with his treating physicians, I examined the patient and other family members. We agreed that the proper diagnosis was posterior polymorphous dystrophy. His nontransplanted left cornea showed typical signs of severe posterior polymorphous dystrophy. These included epithelial and stromal edema, calcific and lipid corneal degeneration, and extensive posterior lesions including thickening of Descemet's membrane and a very irregular posterior surface (Fig 18). In addition, he had broad-based anterior synechiae.

On April 4, 1975, he underwent a 7 mm penetrating keratoplasty OS. There was a problem with elevated intraocular pressure in both eyes along with graft rejection episodes which resulted in gross edema (Fig 19), vascularization (Fig 20), and failure of the transplant OD and borderline success OS when I took over his care on June 19, 1979.

On that date visual acuity was hand motions OD and 20/40 OS. Intraocular pressures were 14 mm Hg OD and 18 mm Hg OS using timolol, epinephrine, and pilocarpine. On July 25, 1979, I performed an 8.5 mm penetrating keratoplasty, intracapsular cataract extraction, and anterior vitrectomy OD. One month later

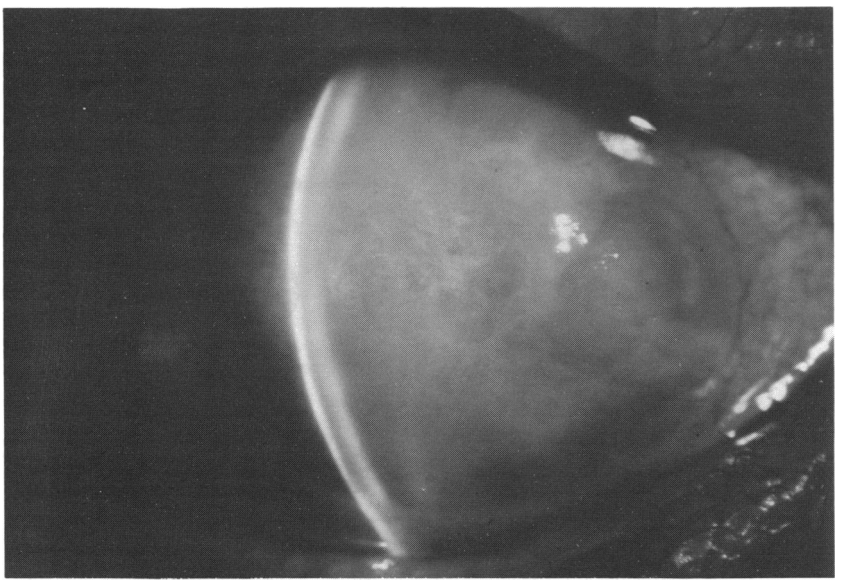

FIGURE 18
Case 8 (Family 3, II-1). Severe PPMD of unoperated left eye. Slit lamp photo demonstrates corneal edema, a thickened posterior layer, stromal scarring, calcific degeneration, and lipid degeneration.

he developed an epithelial and endothelial graft rejection reaction OD. He also had elevated pressure which could not be reduced by maximum medical therapy. Cyclocryotherapy for 180° failed to sufficiently lower the pressure so a trabeculectomy was performed OD on December 15, 1980. The filtering procedure failed. On February 3, 1981, cyclocryotherapy was performed to the superior 180° of the ciliary body. It was repeated inferiorly in April 1981. This finally resulted in well-controlled pressures but the corneal transplant failed with hand motions vision.

The corneal transplant on the left had become edematous with a visual acuity of 20/400. Therefore, on February 22, 1982, an 8 mm penetrating keratoplasty was performed OS. Postoperatively, he developed subepithelial infiltrates which easily cleared with topical steroid therapy. He did not show signs of endothelial rejection. In June 1984, his visual acuity was hand movements OD and 20/30 OS. The corneal transplant was clear OS and he had mild nuclear sclerosis. The right eye was soft and felt to be prephthisical. Intraocular pressure OS was 13 mm Hg.

CASE 9 (FAMILY 3, II-2)

This 64-year-old white woman was first seen by us on November 11, 1975, at the age of 55 years when she presented with a complaint of blurred vision gradually

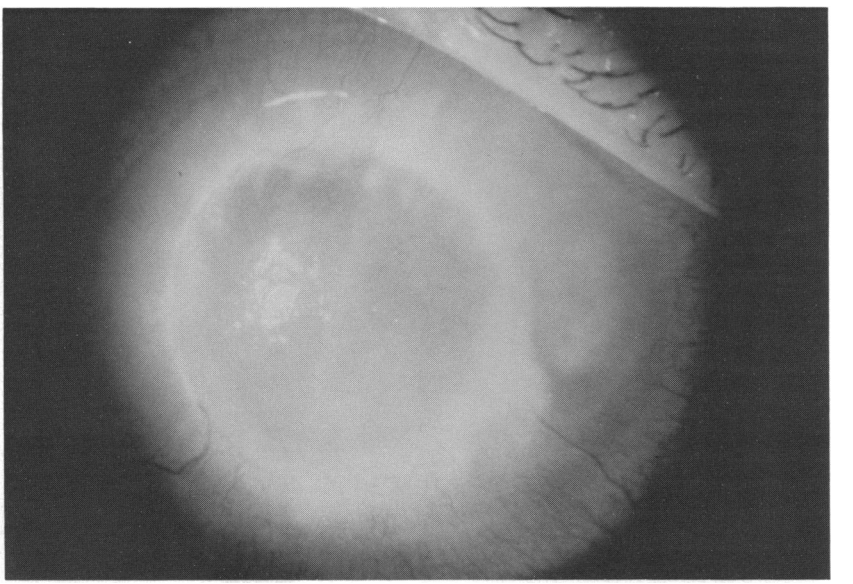

FIGURE 19
Case 8 (Family 3, II-1). Failed corneal transplant OD showing diffuse edema.

worsening over the past 10 years. Visual acuity was counting fingers at two feet OD and counting fingers at three feet OS. Slit lamp examination revealed severe corneal disease with moderate epithelial and stromal edema, calcific degeneration, and a very thickened Descemet's membrane (Fig 21). The posterior corneal surfaces were diffusely irregular. There were iridocorneal adhesions and pupillary ectropion with corectopia due to glass-like membranes on the iris surface bilaterally. She had early nuclear sclerosis OU. Intraocular pressure was 22 mm Hg OU. In November 1975, she underwent a 7.5 mm penetrating keratoplasty OD under local anesthesia. There were no intraoperative complications. The corneal graft cleared over the ensuing 4 months and intraocular pressure was in the low 20s using pilocarpine, epinephrine, and acetazolamide. Unfortunately, the cataract progressed in this eye and in August 1976 the patient underwent an intracapsular cataract extraction with peripheral iridectomy OD. This was complicated by vitreous loss which necessitated an anterior vitrectomy. Intraocular pressure could not be lowered below 35 mm Hg, so in November 1976, she underwent cyclocryotherapy of the right inferior ciliary body with eight applications of −80°C for 60 seconds. The vision gradually improved to 20/400. The optic nerve on the right showed marked glaucomatous cupping and atrophy.

In January 1978, because of increasing intraocular pressure and vision of light perception with good projection OS, the patient underwent a procedure consisting of an 8 mm penetrating keratoplasty, trabeculectomy, and intracapsular cata-

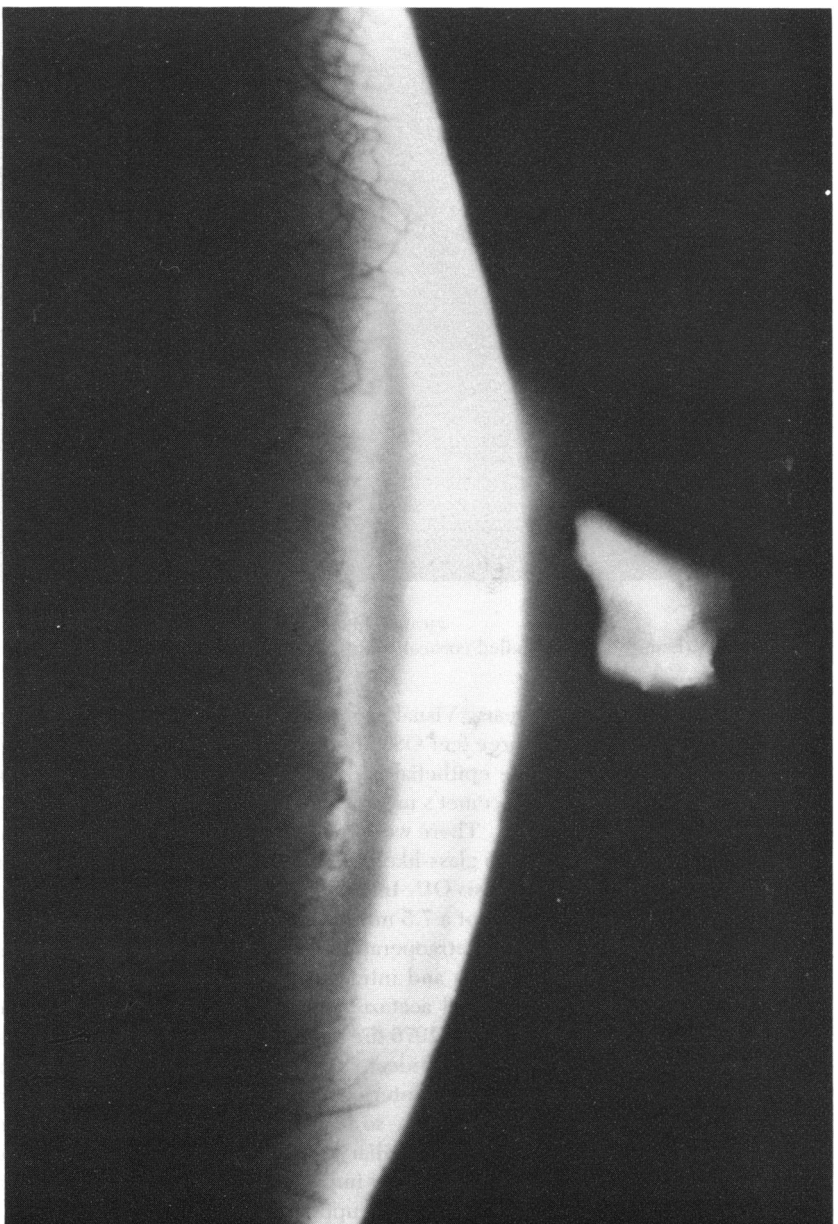

FIGURE 20
Case 8 (Family 3, II-1). Heavy stromal vascularization in failed transplant OD.

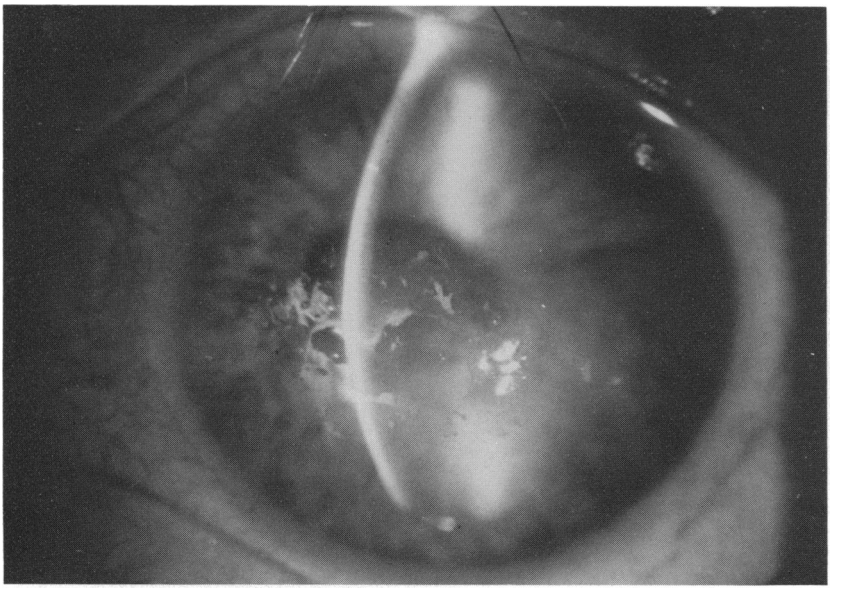

FIGURE 21
Case 9 (Family 3, II-2). Severe PPMD OS demonstrating corneal edema, calcific degeneration, and corectopia.

ract extraction. There were no intraoperative complications. Postoperatively the intraocular pressure could not be controlled on topical and systemic medications. In December 1978, the patient underwent cyclocryotherapy OS because of pressures in the mid 50s. In addition it was noted that a retrocorneal membrane was beginning to form (Fig 22). Again, because of elevated intraocular pressure OS, the patient underwent a trabeculectomy in May 1979. This failed to control the intraocular pressure. The patient subsequently underwent several repeat cyclocryo treatments OS. The retrocorneal membrane OS, which had been noted previously, was slowly advancing to completely cover the posterior surface of the cornea. This was accompanied by the formation of marked microcystic edema, stromal edema, and folds in Descemet's membrane. The edema decreased slightly over the ensuing months.

In December 1984, visual acuity was hand movements OD and the cornea was markedly edematous with a central corneal thickness of 0.91 mm. Visual acuity was 20/400 OS with moderate stromal edema and minimal epithelial edema. There was a dense membrane on the back of the cornea. Corneal thickness was 0.65 mm. Intraocular pressure was 20 mm Hg OD and 12 mm Hg OS.

CASE 10 (FAMILY 3, III-1)

This 39-year-old white man was first seen by us on December 30, 1981, at the age

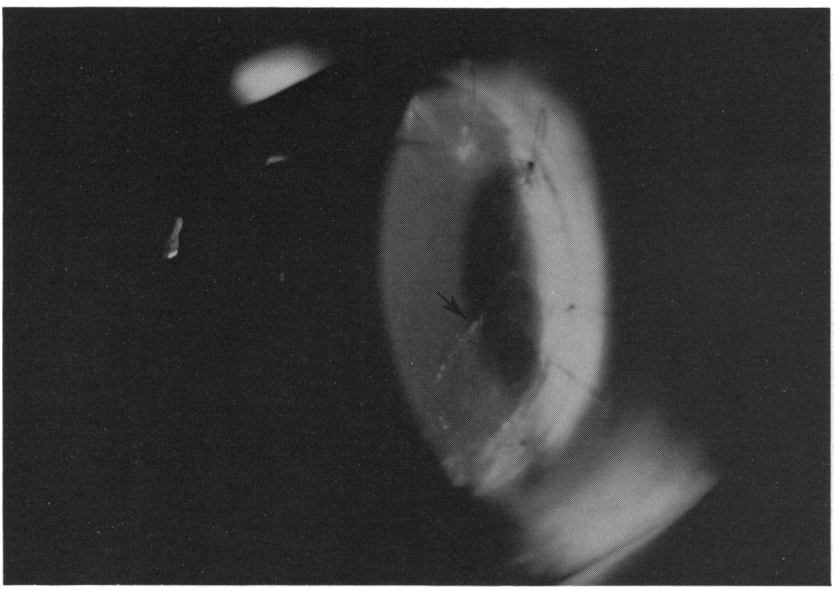

FIGURE 22
Case 9 (Family 3, II-2). Two years postoperative penetrating keratoplasty OS. A retrocorneal membrane was growing from periphery toward center of graft (*arrow points to edge of membrane*).

of 36 years. He presented with a 6-month history of painlessly decreasing vision and marked photophobia OD. The visual acuity was 20/200 OD and 20/20 OS. Examination of the right cornea showed moderate disease. He had slight epithelial edema and moderate central stromal edema (Fig 23). The posterior corneal surface was very irregular and contained large patches of thickened tissue. Peripheral iris adhesions to the posterior surface of the cornea were seen by slit lamp examination. The left cornea also had endothelial changes of PPMD but there was no stromal or epithelial edema. There was one small area of iris adhesion to the posterior corneal surface. Intraocular pressures were 22 mm Hg OD and 16 mm Hg OS. At this time timolol was started in the right eye, in an attempt to decrease the edema and thereby improve his vision. Intraocular pressure in the right eye was controlled. However, 1 year later the patient developed painful epithelial edema necessitating a bandage contact lens OD.

By February 1983, visual acuity had decreased to approximately counting fingers at five feet OD because of bullous keratopathy. On February 23, 1983, the patient underwent an 8 mm penetrating keratoplasty under local anesthesia. There were no intraoperative complications. Two months after surgery the patient's intraocular pressure had risen to 40 mm Hg OD. Timolol and acetazolamide were started and the pressure was reduced to 15 mm Hg. In August 1983,

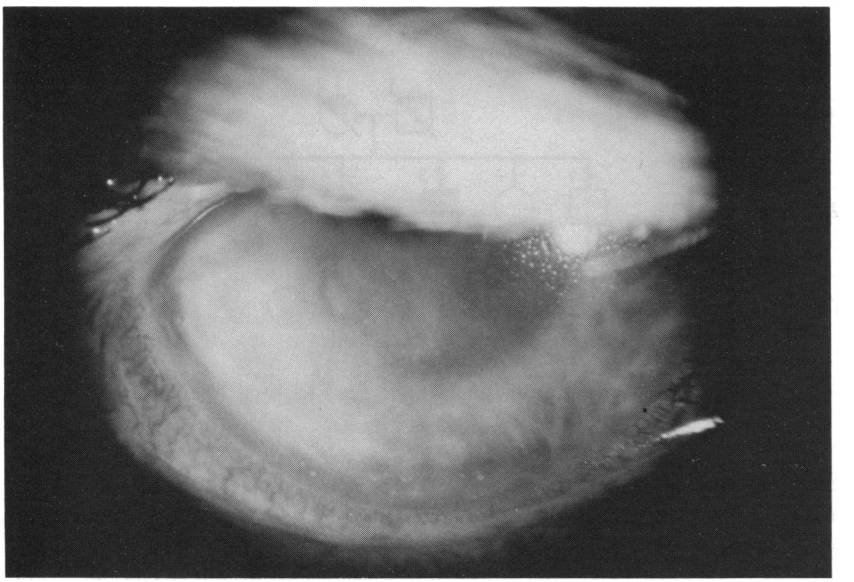

FIGURE 23
Case 10 (Family 3, III-1). Preoperative photo slit lamp picture showing diffuse corneal edema and opacities OD. Patient was extremely photophobic, a characteristic of many patients with advanced PPMD.

subepithelial infiltrates, keratic precipitates, and a moderate anterior chamber inflammation were seen. He was started on high dose topical steroid drops which resolved the graft rejection. The patient was gradually tapered off his steroid drops. In addition, acetazolamide was discontinued when it was found that the pressure could be controlled on timolol. In May 1984, the pressure increased to 32 mm Hg so dipivefrin was begun. This reduced the pressure to 27 mm Hg and pilocarpine was added. In November 1984, the best-corrected visual acuity was 20/40 and the intraocular pressure was 25 mm Hg.

CASE 11 (FAMILY 4, III-4)

This 60-year-old white man was first seen by us on March 31, 1975, when he was 50 years old with a complaint of poor vision OD for as long as he could remember and gradual painlessly decreasing vision OS for the last 2 years (Fig 24). On examination the visual acuity was counting fingers at one foot OD and 10/200 OS. Intraocular pressures, measured with a Goldmann applanation tonometer, were approximately 20 mm Hg OD and 12 mm Hg OS. Examination of the cornea OD revealed severe disease which included calcific and lipid degeneration and diffuse microcystic and stromal edema (Fig 25). Descemet's membrane was so thickened that it appeared as white fibrous tissue. The left cornea also had microcystic

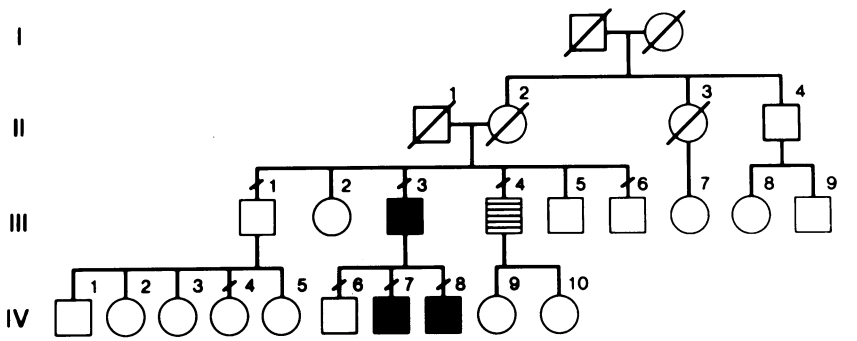

FIGURE 24
Pedigree of Family 4 (see Fig 1 for key).

edema and band keratopathy (Fig 26). There was mild stromal edema. Descemet's membrane had typical posterior polymorphous changes consisting of isolated vesicles and areas of gray thickening. No iridocorneal adhesions were noted. On May 17, 1975, when vision was counting fingers at three feet OD, an 8 mm corneal transplant under local anesthesia was performed. There were no intraoperative complications. Postoperatively the pressure was well-controlled without medications.

Visual acuity OS remained at 20/400. On June 16, 1976, the patient underwent an 8 mm penetrating keratoplasty OS under local anesthesia. He had a graft rejection episode in December 1976, characterized by keratic precipitates and a moderate anterior chamber reaction. This was successfully treated with topical steroids. Visual acuity in January 1984, was 20/80 OD and 20/40 OS with moderate nuclear sclerotic cataracts and clear corneal transplants OU. Intraocular pressure was 16 mm Hg OU.

CASE 12 (FAMILY 5, II-5)

This 61-year-old white man was first seen by us on November 18, 1980 when he was 57 years old (Fig 27). He was referred with a complaint of painless decrease in visual acuity, greater OS than OD, over the previous 1½ years. Visual acuity was 20/30 OD and 20/100 OS. Slit lamp examination showed moderate disease OU. The right eye had an extremely slight haziness of the epithelium, mild stromal edema and an irregular posterior surface. The left cornea had microcystic and stromal edema. There was corectopia OU (Fig 28). Specular microscopy of the posterior layer of both corneas revealed islands of abnormal cells next to normal appearing endothelial cells (Fig 29). By gonioscopy, broad peripheral anterior synechiae were seen extending to Schwalbe's ring for about 90° of the anterior chamber angle OU (Fig 30). One son also demonstrated posterior corneal lesions but fine iridocorneal adhesions (Figs 31 and 32). Intraocular pressure was 19 mm

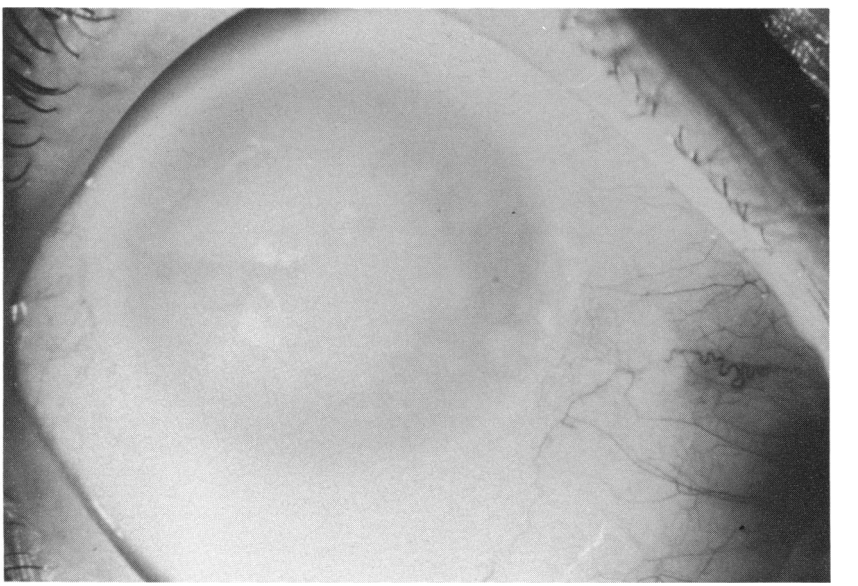

FIGURE 25
Case 11 (Family 4, III-4). Severe PPMD OD demonstrating diffuse edema, scarring, and calcific and lipid corneal degeneration OD.

Hg OD and 26 mm Hg OS. In the hope that lowering of the intraocular pressure on the left would improve the vision, the patient was started on timolol. One month later he actually had increased epithelial and stromal edema with a pressure of 20 mm Hg OS. It was also better appreciated that the patient had a moderate nuclear sclerotic cataract OS. Intraocular pressure was 22 mm Hg OD. Timolol was begun on the right.

On January 12, 1981, with a visual acuity of 20/300 OS, the patient underwent an 8 mm penetrating keratoplasty and an intracapsular cataract extraction under local anesthesia. The vitreous face bulged so that the donor button could not be sutured without performing an anterior vitrectomy. Postoperatively the patient had no complications and his pressure was well-controlled on timolol. Visual acuity through a hard contact lens was 20/25. The corneal edema OD continued to worsen, and on July 7, 1982, when the visual acuity was 20/100, that eye underwent an 8 mm penetrating keratoplasty and intracapsular cataract extraction and anterior vitrectomy under local anesthesia. There were no intraoperative complications. Because of an elevated postoperative pressure of around 30 mm Hg OD, acetazolamide was added to timolol for pressure control. This regimen maintained intraocular pressure at about 20 mm Hg. In February 1983 the acetazolamide was discontinued, and it was found that the patient's intraocular pressure remained at

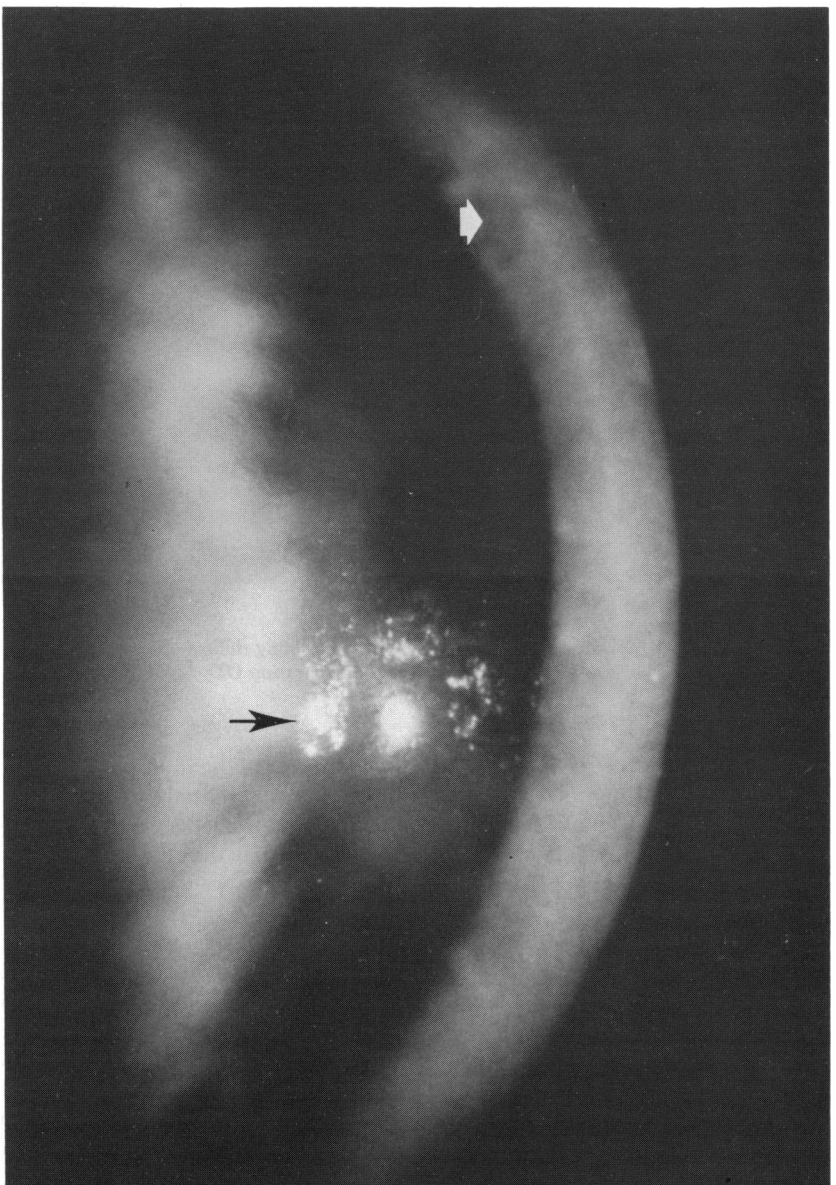

FIGURE 26
Case 11 (Family 4, III-4). Preoperative photo OS demonstrating calcific degeneration (*black arrow*) and posterior pathology (*white arrow*).

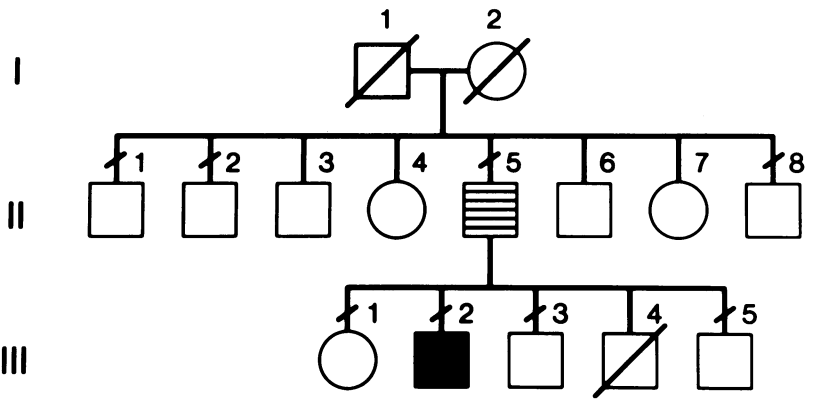

FIGURE 27
Pedigree of Family 5 (see Fig 1 for key).

an acceptable level. He successfully wears hard contact lenses OU and on September 20, 1984, his visual acuity was 20/25 OU.

CASE 13 (FAMILY 6, III-4)

This 49-year-old white man was first seen by us on April 17, 1974, when he was 39 years old (Fig 33). He complained of painlessly decreasing vision OU for the last 2 years. At another institution, the diagnosis of Cogan's microcystic dystrophy was made. The patient had been treated with epithelial scraping and a soft contact lens OS. When we examined him, his visual acuities were 20/30 OD and 20/60 OS. Examination of his right cornea revealed epithelial blebs as well as fingerprints. The stroma, Descemet's membrane, and endothelium appeared normal. The left cornea revaled an irregular epithelial surface with minimal stromal edema and a beaten-metal appearance of the endothelium. Failing to see endothelial lesions at that visit, we also misdiagnosed the patient as an anterior instead of posterior membrane dystrophy.

The patient returned 2 years later with a complaint of decreased vision OD. We were able to make the correct diagnosis at the time. Visual acuity was 20/100 OD and 20/50 OS. Both corneas demonstrated moderate disease. The right cornea revealed epithelial blebs and fingerprints as before (Fig 34). There was mild stromal thickening as well as a beaten-metal appearance of the endothelium with areas of thickening of Descemet's membrane. Specular microscopy, performed 3 years later, revealed islands of abnormal-appearing cells and dark spots within the endothelial mosaic (Fig 35). The left cornea also had mild stromal edema with some thickening of Descemet's membrane. Intraocular pressure was 18 mm Hg OD and 16 mm Hg OS by Goldman applanation. No iridocorneal adhesions were noted.

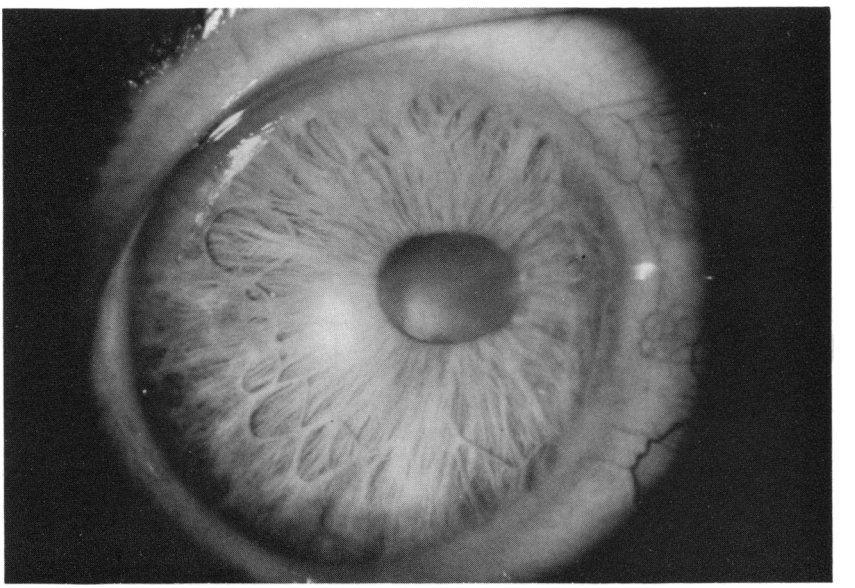

FIGURE 28
Case 12 (Family 5, II-5). Preoperative slit lamp photo OD demonstrating corneal edema and corectopia.

On January 18, 1978, with a visual acuity of 20/80 OD, the patient underwent an 8 mm penetrating keratoplasty under local anesthesia. There were no intraoperative complications. Postoperatively the intraocular pressure was well controlled without medication. The left eye subsequently developed painful bullous keratopathy (Fig 36). In June 1979, with a visual acuity of 20/70, the patient underwent an 8 mm penetrating keratoplasty OS under local anesthesia. There were no intraoperative complications. Fourteen months following the corneal transplant OS, the patient had a graft rejection characterized by subepithelial infiltrates and moderate anterior chamber inflammation. This was successfully overcome by the use of topical steroids. Besides this one episode of rejection the patient had no other postoperative complications in either eye. His best-corrected visual acuity in June 1983 was 20/30 OD and 20/20 OS.

LABORATORY

I performed 22 corneal transplants on 20 eyes of 13 patients with PPMD from 1974 through 1984. In each case, vision was reduced primarily because of corneal edema. The edema was both corneal and, more importantly, epithelial. Trabeculectomy surgery was performed by Dr Charles D. Phelps. Trabecular meshwork and iris tissue obtained for study came

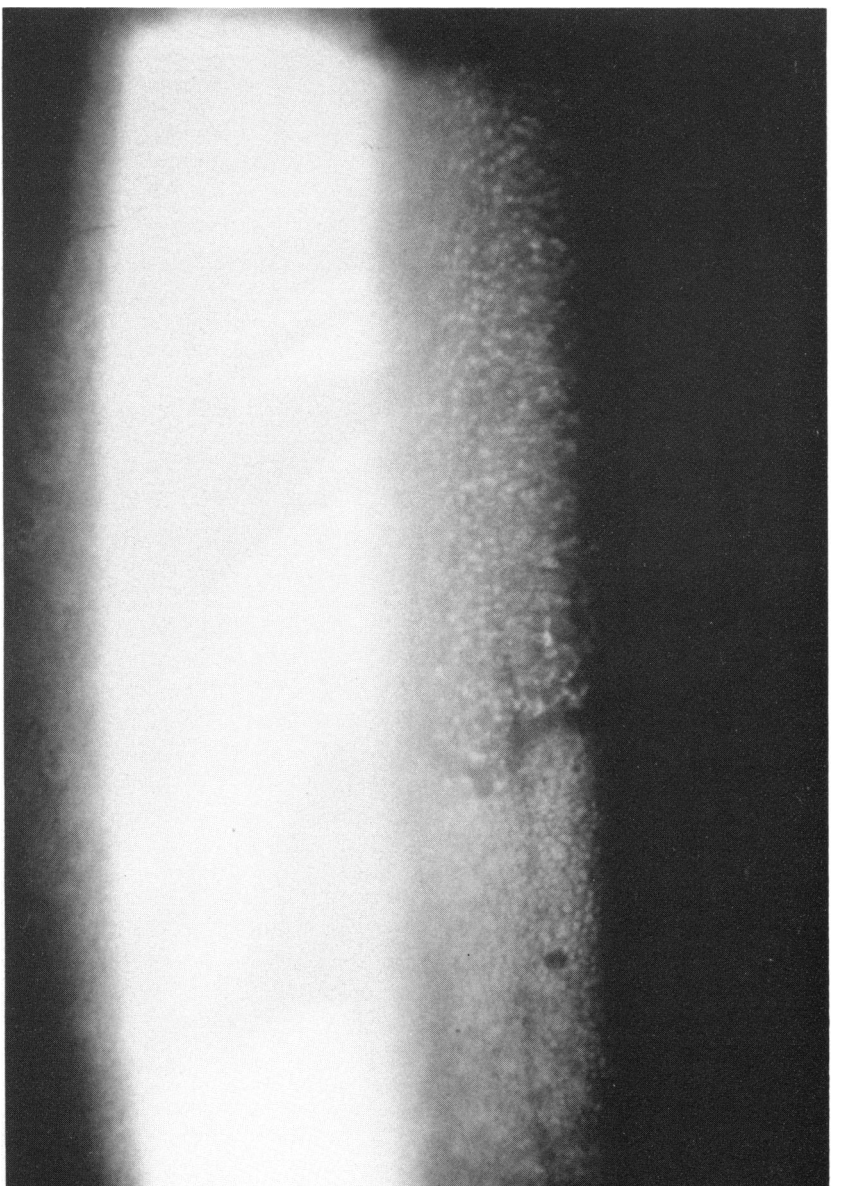

FIGURE 29
Case 12 (Family 5, II-5). Specular photomicrograph showing a large area of abnormal cells adjacent to a rather normal endothelial mosaic OD.

FIGURE 30
Case 12 (Family 5, II-5). Gonioscopy photo OS demonstrating broad-based iridocorneal adhesions (*arrow*) which could not be seen grossly by slit lamp examination.

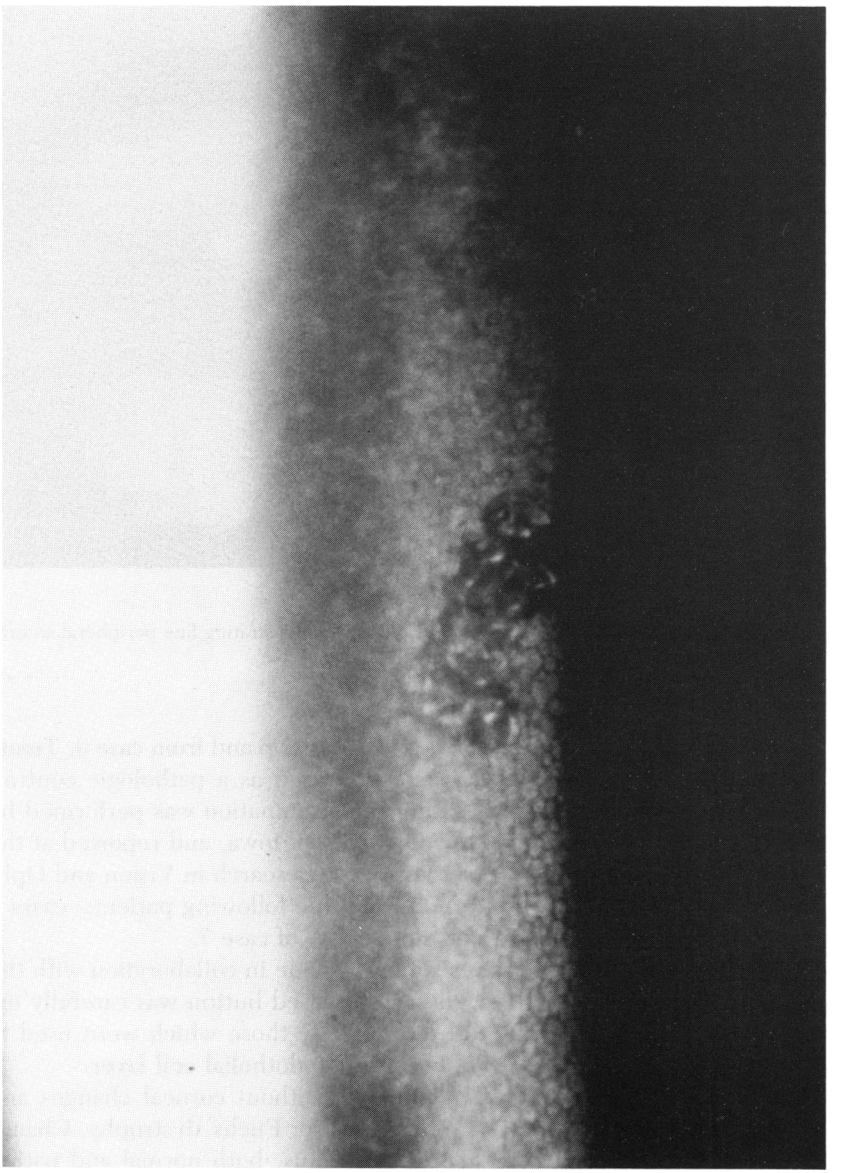

FIGURE 31
Twenty-six-year-old son (Family 5, III-2) of case 12 with islands of abnormal posterior cells adjacent to normal-appearing endothelial cells OD documented by specular photomicroscopy.

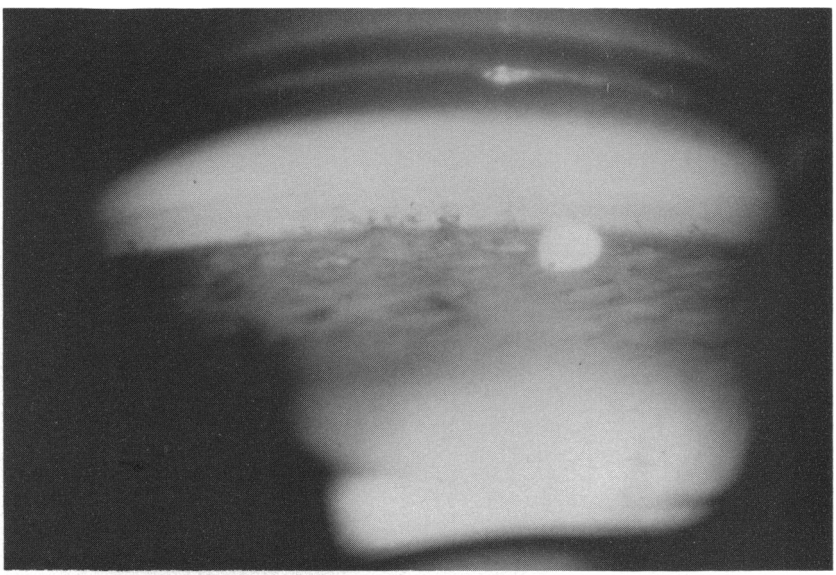

FIGURE 32
Twenty-six-year-old son (Family 5, III-2) of case 12 demonstrating fine peripheral anterior synechia on gonioscopy OS.

from the 48-year-old son (family 2, IV-3) of case 6 and from case 9. Tissue from a case of Chandler's syndrome was used as a pathologic control. From 1974 through 1976, the pathologic examination was performed by Dr Thomas A. Weingeist, at the University of Iowa, and reported at the 1976 Annual Meeting of the Association for Research in Vision and Ophthalmology. The specimens were those of the following patients: cases 1 (both eyes), 2, 3, 4, 7, 8, 9, and the brother of case 7.

After that time, laboratory research was done in collaboration with the National Eye Institute. Although each diseased button was carefully examined in the laboratory, I will discuss only those which were used to extensively characterize the nature of the endothelial cell layer.

Controls included fresh eye bank eyes without corneal changes and buttons removed at the time of keratoplasty for Fuchs' dystrophy, Chandler's syndrome, and interstitial keratitis. Thus, both normal and pathologic corneas were used as controls. After each corneal button was removed from the recipient, a technician was standing by in the operating room to section the specimens and then place a piece of culturing in McCarey-Kaufman solution with gentamycin, a piece for light microscopy

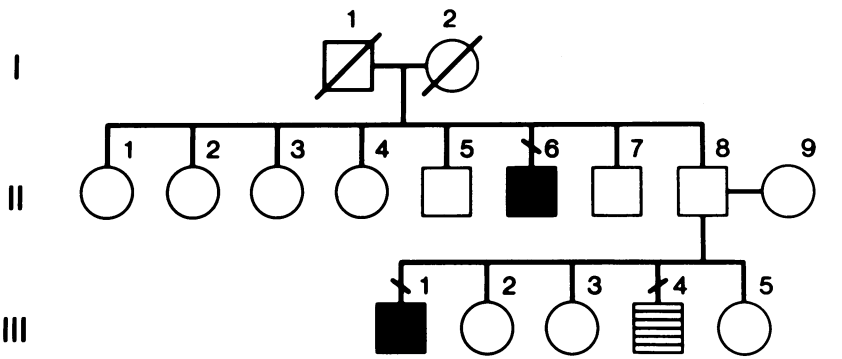

FIGURE 33
Pedigree of Family 6 (see Fig 1 for key).

in formalin, and a piece for electron microscopy in glutaraldehyde. Specimens for immunologic studies were fast-frozen with dry ice.

The tissue was flown that day or the following day to the National Eye Institute in Bethesda, Maryland. Histopathologic examination was performed by Dr Merlyn M. Rodrigues. Cell culture studies were done by Dr David A. Newsome, now of the Johns Hopkins University School of Medicine. Keratin staining examination was done in conjunction with Dr Tung-Tien Sun, also of the Johns Hopkins University School of Medicine and now of New York University School of Medicine, New York City. Reported tissue culture and keratin staining results came from cases 6, 9, and 13.

The photograph of the specimen in Fig 41 came from the laboratory of Dr Weingeist. Those from Figs 37 to 40 and 42 to 46 came from the laboratories of Drs Rodrigues, Newsome, and Sun.

For routine light microscopy, the formalin fixed paraffin embedded tissues were stained with hematoxylin-eosin and periodic acid-Schiff (PAS). To prepare specimens for transmission electron microscopy, they were fixed in 2.5% buffered glutaraldehyde, postfixed in osmium tetroxide, dehydrated in ascending concentrations of alcohol, and embedded in epon. For scanning electron microscopy, the specimens were fixed in buffered glutaraldehyde in graded acetone, critical point dried and coated with gold palladium.

In order for tissue culture studies to be performed, Descemet's membrane with associated endothelial cells was dissected from controls and PPMD corneas under a dissecting stereomicroscope. In the PPMD cases,

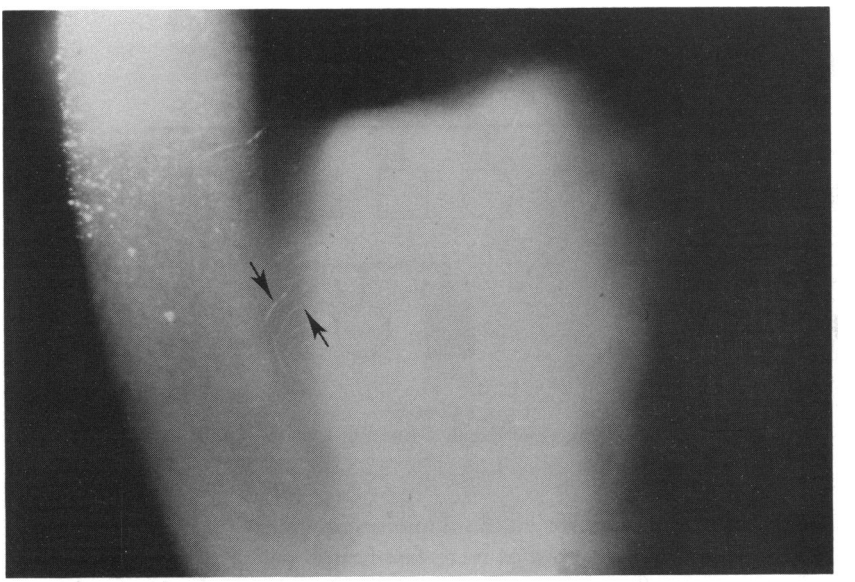

FIGURE 34
Case 13 (Family 6, III-4). Preoperative slit lamp photo OD demonstrating epithelial edema with fingerprint-like lines (*arrows*).

Descemet's membrane adhered only weakly to the stroma, thus permitting easy and clean separation. Explants of corneal endothelium were placed onto Petri dishes with the stromal side (anterior portion of Descemet's membrane) down. In addition to explants of endothelium those of stroma and epithelium from both controls and PPMD corneas were maintained in 60 mm polystyrene dishes with 3 ml Eagle's modified essential medium containing 5% fetal calf serum, penicillin (100 mg/ml), and streptomycin (50 mg/ml). The dishes were incubated at 37°C in an atmosphere of 95% air, 5% CO_2, and 100% humidity. Tissue culture media was changed every 3 to 4 days.

Antibodies prepared against a group of keratins purified from human stratum corneum[9,10] were used to identify epithelial cells containing keratins by immunofluorescence.[11] The antiserum against the keratin fraction was characterized by immunoelectrophoresis with sodium dodecyl sulfate slab gel and contained antibodies against all the major electrophoretic bands of keratins.[11] For immunofluorescent staining,[12] frozen sections (6 μ thick) were prepared. The air-dried tissue sections were hydrated in phosphate-buffered saline (PBS) and covered with 20 ml of

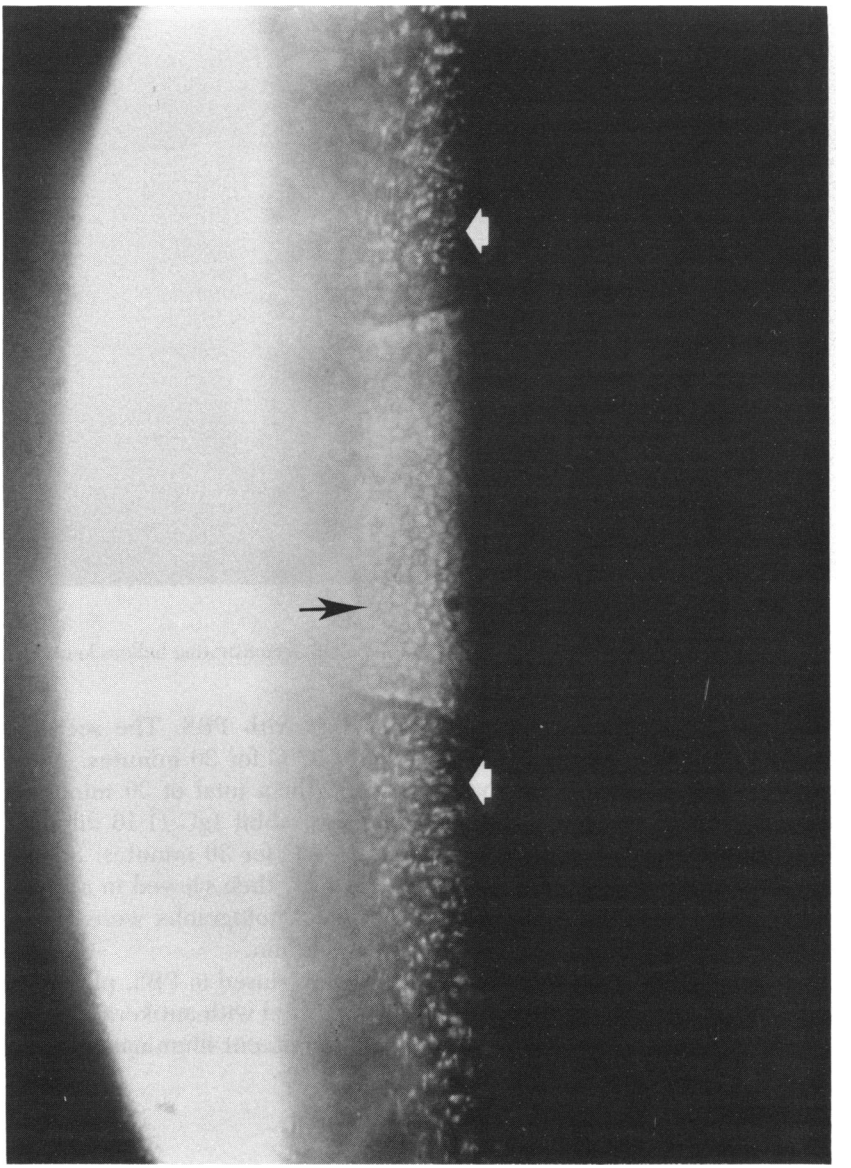

FIGURE 35
Case 13 (Family 6, III-4). Specular photomicrograph OD demonstrating two large abnormal posterior corneal areas (*white arrows*) with intervening endothelial cells which are grossly normal (*black arrow*).

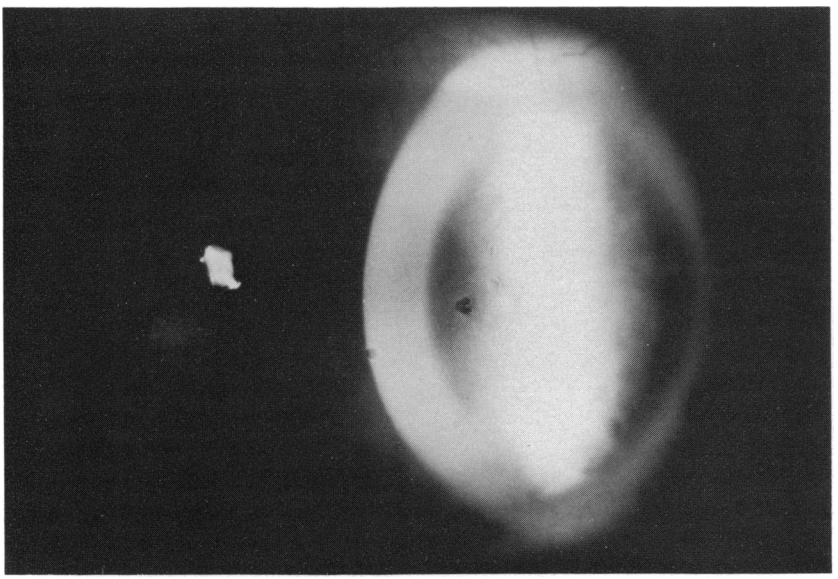

FIGURE 36
Case 13 (Family 6, III-4). Preoperative slit lamp photo OS demonstrating bullous keratopathy.

antikeratin antiserum previously diluted 1:48 with PBS. The sections were incubated in a humidified chamber at 37°C for 30 minutes. They were then washed in three changes of PBS for a total of 30 minutes, overlaid with fluorescein-conjugated goat anti-rabbit IgG (1:16 diluted; Miles Laboratories, Inc.) and incubated at 37°C for 30 minutes. Specimens were rinsed again, mounted in Gelvatol,[13] then viewed in a Leitz Orthoplan microscope with epi-illumination. Photographs were taken with Ektachrome 400 ASA film with Tri-X pan film.

Cultured endothelial and epithelial cells were rinsed in PBS, placed in methanol, chilled to −20°C for 5 minutes, reacted with antikeratin antiserum as described,[11] and viewed with epifluorescent illumination.

RESULTS

LABORATORY

Tissue Specimens

1. *Light Microscopy*: Varying amounts of stromal and epithelial edema were observed in all the PPMD corneal specimens examined. The cor-

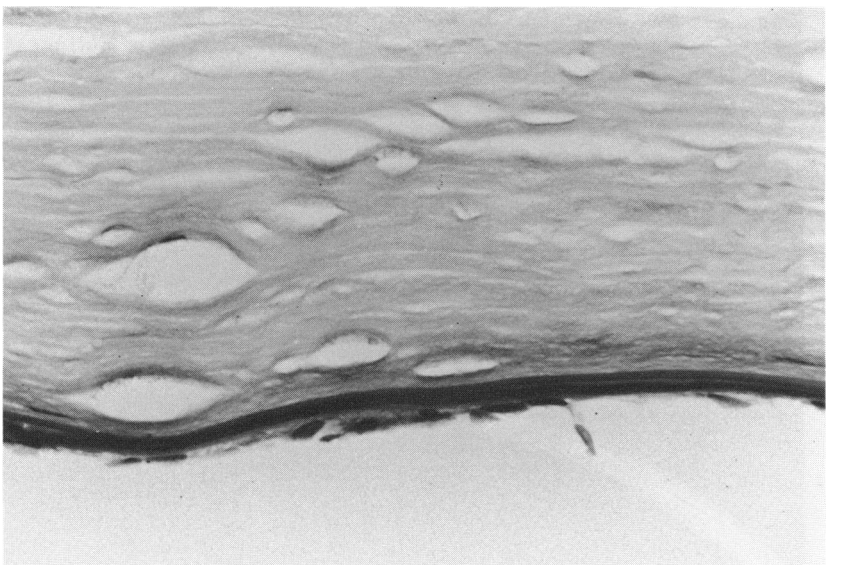

FIGURE 37
Case 9 (Family 3, II-2). PPMD cornea demonstrating multilaminar Descemet's membrane on light microscopy (× 165).

neal endothelium was either a monolayer or a double layer of cells lining the posterior surface of Descemet's membrane. Descemet's membrane appeared multilayered and demonstrated marked irregularity in its thickness (Fig 37). The stromal collagent and the keratocytes were unremarkable. Light microscopy of trabecular meshwork and iris specimens from PPMD cases revealed a multilayered membrane continuing from the cornea and growing down over these structures.[14]

2. *Antikeratin Staining*: Indirect immunofluorescent staining of the PPMD corneal endothelial tissue with guinea pig antisera against total human epidermal keratins and individual purified human keratins (MS 65K, 63K, 55K, and 46K),[15] as well as a mouse monoclonal antibody specific for several low molecular weight human epidermal keratins[16] revealed staining of the epithelial-like cells on the posterior corneal layer that corresponded to areas of epithelial-like cells demonstrated by scanning and transmission electron microscopy (Fig 38). In the PPMD specimens there were patches of endothelium that did not stain with antikeratin antibodies. Presumably these areas represented normal endothelial cells.[17] The epithelium stained with total human epidermal keratins in all

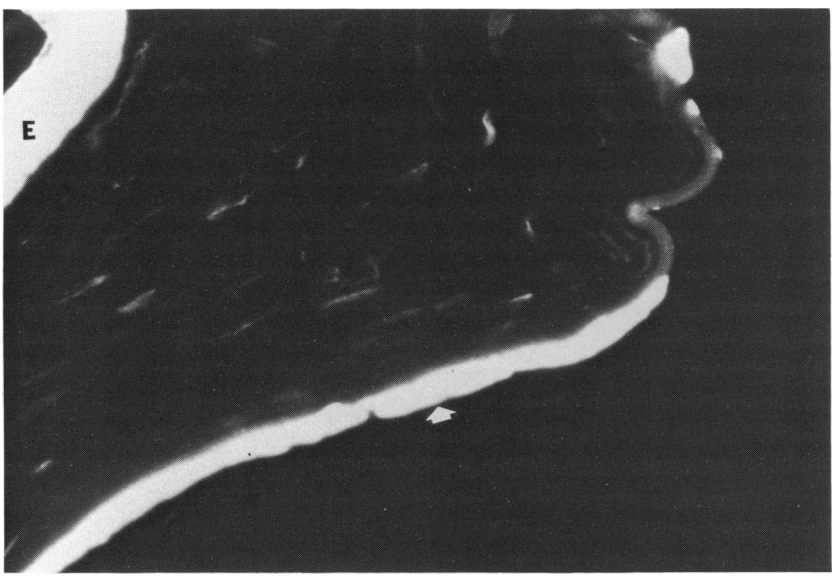

FIGURE 38
Case 13 (Family 6, III-4). Corneal tissue. Positive antikeratin antibody staining of epithelium (E). Pathologic staining of epithelial-like cells on posterior surface of cornea (*arrow*). Areas with lack of staining on posterior surface do not contain epithelial-like cells (× 100).

specimens. The stroma of PPMD corneas and controls did not stain for keratin. The endothelium of the normal and pathologic controls also did not stain for keratin.[18] Trabecular meshwork and iris specimens from PPMD were not tested for staining.

3. *Scanning Electron Microscopy*: Two populations of cells were observed in all PPMD specimens by scanning electron microscopy of the corneal endothelium (Fig 39). Some areas contained epithelial-like cells and others contained endothelial-like cells.[17] The endothelial-like cells were characterized by a polygonal appearance of fairly uniform cells with the usual junctional complexes, while the epithelial-like cells were much larger and squamoid in appearance with numerous microvillous projections.

4. *Transmission Electron Microscopy*: The stroma and epithelium showed edema but the outstanding features were found in the endothelium and Descemet's membrane (Fig 40).[17,19,20]

The endothelium was characterized by the appearance of four different cell types. "Normal" appearing cells were observed in some areas. Far

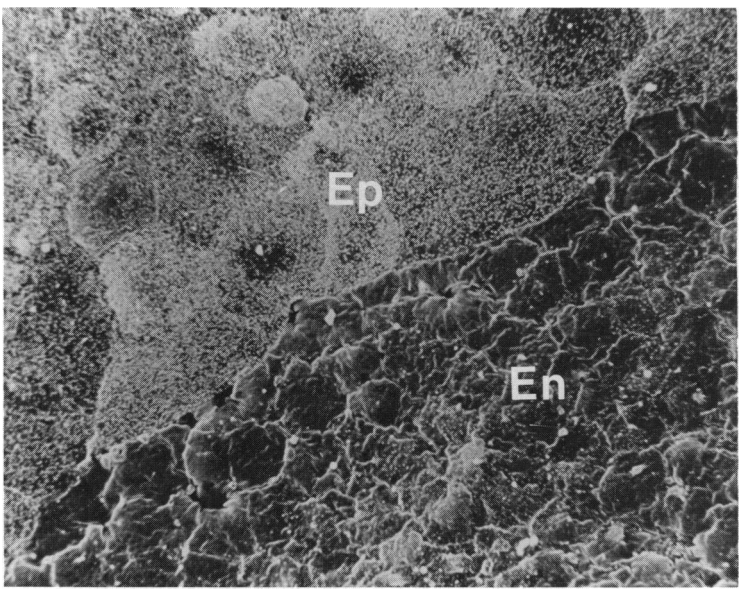

FIGURE 39
Case 9 (Family 3, II-2). Scanning electron photomicrograph of corneal tissue demonstrating two populations of cells. One type represents endothelial cells without epithelial-like characteristics (En). The other type has epithelial-like characteristics with numerous microvillous projections (Ep) (× 1400).

more common was the occurrence of epithelial-like cells, fibroblast-like cells, and degenerating endothelial cells characterized by attenuation and vacuolization. The epithelial-like cells were multilayered and contained numerous desmosomes, microvillous protrusions, and 8 to 10 nm diameter cytoplasmic filaments.

Descemet's membrane was found to be highly variable and in part related to the age of the patient. The corneas from young patients tended to have a normal appearing anterior banded portion followed immediately by a highly abnormal posterior nonbanded portion. Older patients demonstrated a normal anterior banded portion followed immediately by a rather normal appearing nonbanded portion. The normal nonbanded posterior portion was usually narrow and then became pathologic demonstrating a multilaminar appearance with abnormal posterior banding, closely packed collagen fibrils 8 to 10 nm in diameter sandwiched between normal appearing Descemet's layer, and occasional cells with and without basal lamina. Cornea guttata were occasionally seen within the

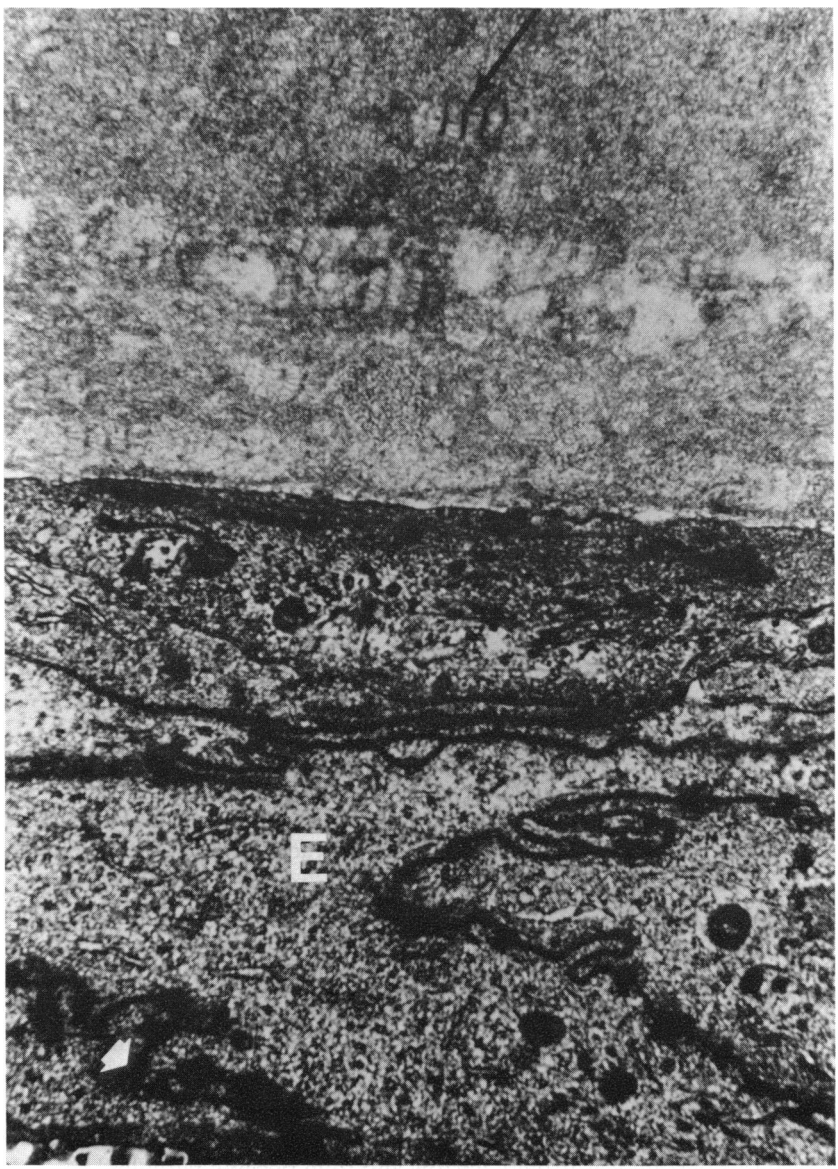

FIGURE 40
Case 9 (Family 3, II-2). Transmission electron photomicrograph of corneal tissue showing abnormal posterior Descemet's banding (*black arrow*), multilaminar endothelium (E), desmosomal junctions between endothelial cells (*white arrow*), and microvillous projections from endothelial surface into anterior chamber (× 8000).

FIGURE 41
Case 1 (Family 1, V-3). Corneal tissue demonstrating a gutta consisting of dense homogeneous basal lamina and whorls of collagen fibrils buried in Descemet's layer (*arrow*) (× 18,000).

FIGURE 42
Forty-six-year-old son (Family 2, IV-3) of case 6. Trabecular meshwork specimen obtained at time of trabeculotomy. Endothelial membrane extending down from cornea across inner surface of trabecular meshwork (*arrow*). Membrane is multilayered (× 130).

pathologic Descemet's layer (Fig 41). They varied from homogenous excrescences to dense homogenous looking basal lamina substance combined with whorls of collagen fibrils. The distance between the anterior banded border of Descemet's layer and the posterior cell layer varied greatly in PPMD. Even within the same specimen, this distance was from 3 to 30 μ.

Transmission electron microscopy of trabecular meshwork specimens from PPMD cases revealed that the extension of "endothelial" cells from the cornea over the inner trabecular meshwork in fact were more like epithelial cells (Fig 42). These cells were multilayered, exhibited microvilli, desmosomal attachments, scant mitochondria, and cytoplasmic filaments. Basement membrane material and collagen resembling Descemet's membrane were irregularly seen between the membrane and trabecular meshwork.

Transmission electron microscopy of iris specimens from PPMD patients also revealed an epithelial-like cellular membrane covering the surface (Fig 43). Further examination of these cells revealed that they

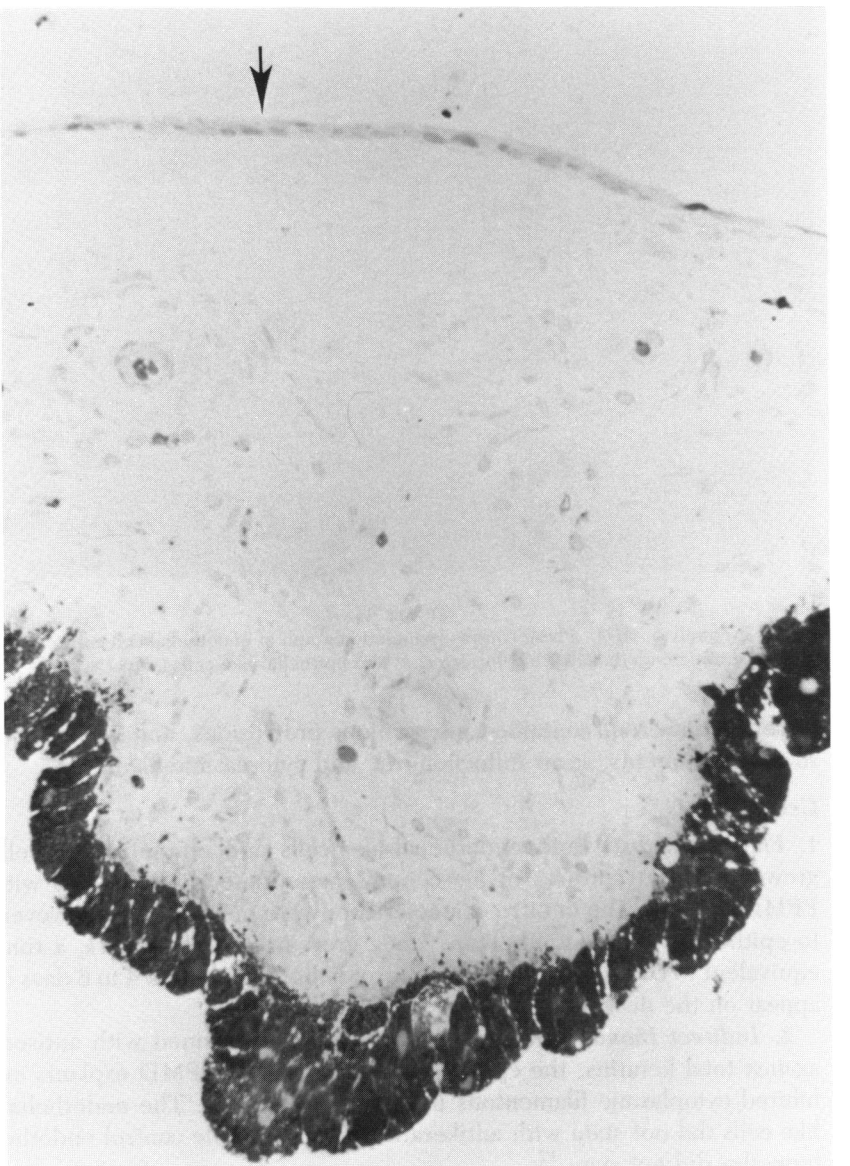

FIGURE 43
Case 9 (Family 3, II-2). Iris specimen obtained at time of combined trabeculectomy, sector iridectomy, and penetrating keratoplasty. A multilayered membrane grows across anterior surface of iris (*arrow*) (× 120).

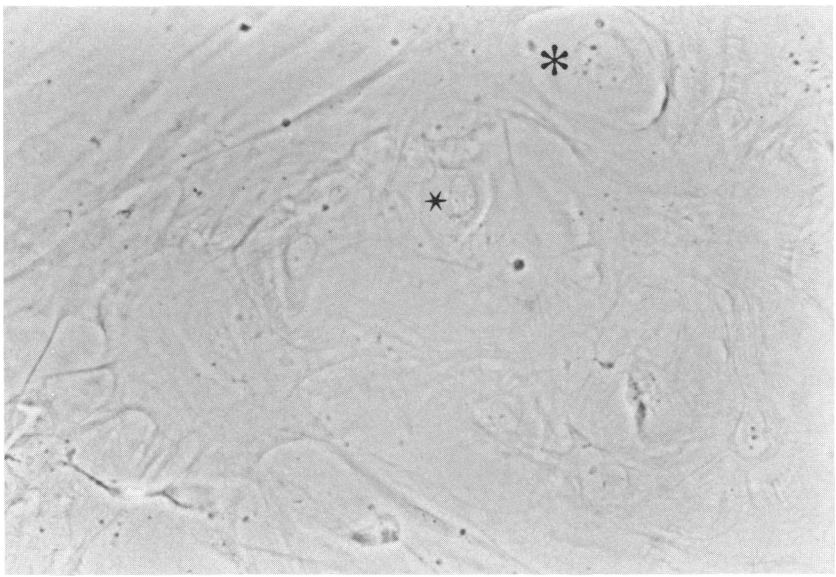

FIGURE 44
Case 13 (Family 6, III-4). Phase contrast photomicrograph of endothelial cell culture demonstrating endothelial-like cells (*asterisk*) and epithelial-like cells (*star*) (× 154).

were multilayered, contained microvillous protrusions, and had desmosomal attachments, scant mitochondria, and cytoplasmic filaments.

Cell Cultures

1. *Phase-Contrast*: Both endothelial-like cells and epithelial-like cells grew in explant cultures of Descemet's membrane from patients with PPMD (Fig 44). The *in vitro* characteristics were more similar, however, to epithelium than endothelium. They grew in 24 to 48 hours, a time equivalent to control epithelium. Control endothelium took 4 to 6 days to appear on the dish.[18]

2. *Indirect Immunofluorescent Staining*: When stained with antisera against total keratins, the epithelial-like cells of the PPMD explants exhibited cytoplasmic filamentous fluorescence (Fig 45). The endothelial-like cells did not stain with antikeratin antibodies. The control endothelium also did not stain.[17]

3. *Scanning Electron Microscopy*: Two populations of cells grown in culture were also identified by scanning electron microscopy. The predominant difference was that some had only occasional microvillous projections while others were covered by a myriad of microvillous pro-

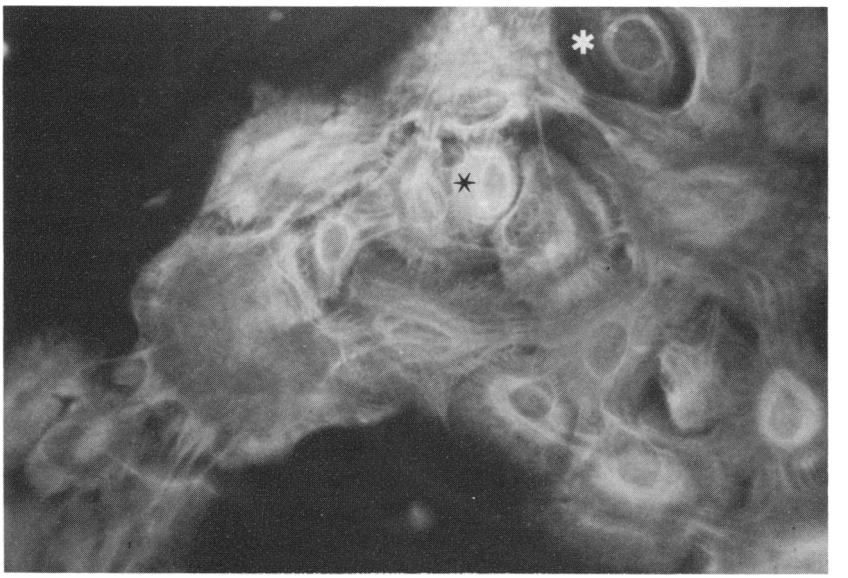

FIGURE 45
Case 13 (Family 6, III-4). Phase contrast photomicrograph of keratin staining of cell culture from corneal endothelium. Epithelial-like cells (*star*) stain with total human epidermal keratin. Endothelial-like cells (*asterisk*) do not stain for keratin (× 100).

jections. Those cells with numerous microvilli were felt to represent epithelial-like cells.[18]

4. *Transmission Electron Microscopy*: The predominant cell grown in culture from PPMD buttons was an epithelial-like cell with microvillous projections, desmosomal junctions, prominent Golgi, moderate mitochrondria, and smooth endoplasmic reticulum (Fig 46). They contained 8 to 10 nm cytoplasmic filaments similar to epithelial cells grown in culture. The cultures grew in a stratified 2 to 3 layer pattern similar to that seen in the buttons. Occasional fibroblast-like cells with prominent dilated rough endoplasmic reticulum were also found.[18]

CLINICAL

The number of cases and the great number of variables (severity of corneal disease, severity of iris disease, severity of glaucoma, multiple previous surgeries) makes statistical analysis inappropriate. General statements using percentages, however, seem applicable. A total of 22 corneal transplants done on 20 eyes of 13 patients is included in this study

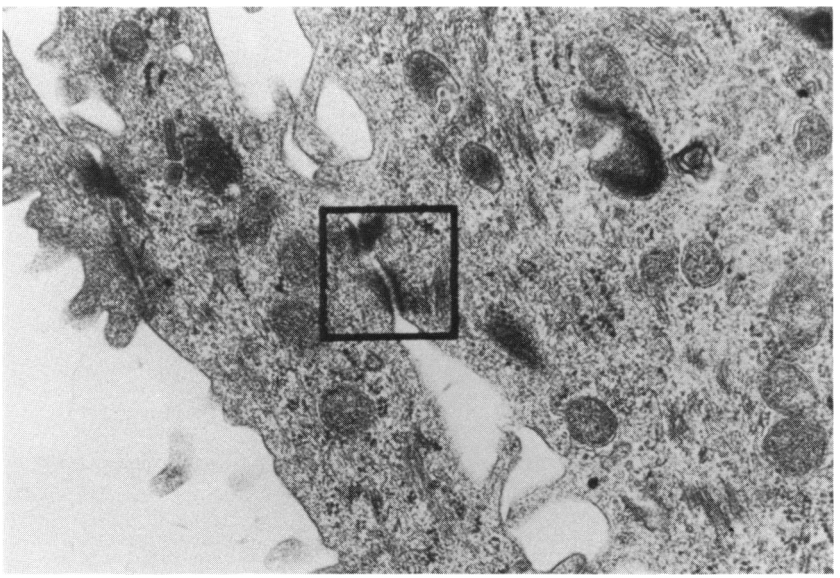

FIGURE 46
Case 6 (Family 2, III-1). Transmission electron photomicrograph of cell culture from posterior polymorphous dystrophy endothelium. Cells are epithelial-like exhibiting same characteristics as in corneal button. These include cytoplasmic keratin filaments, desmosomal junctions (*box*), multilaminar arrangement, and microvillous projections (× 44,000).

(Table I). Seven patients had bilateral corneal transplants. Two patients required a repeat corneal transplant on one eye because of corneal graft failure. Four transplants (case 4 OS, case 5 OS, case 8 OU) were done on eyes that had corneal transplant surgery before I took over care of the patient.

Nine (69%) were males and four (31%) were females. Eleven (50%) of the operated eyes were right eyes, and 11 (50%) were left eyes. The age range of this group at the time of surgery was 11 to 77 years, with an average age of 46 years. The follow-up time for an operated eye ranged from 4 months (case 6) to 9 years with an average of 4.75 years.

As shown in Table I, the preoperative visual acuity varied from 20/70 to light perception. Four eyes had a preoperative visual acuity between and including 20/80 to 20/100, 7 eyes were in the range of 20/120 to 20/400, and 11 eyes had an initial visual acuity worse than 20/400.

Severity of corneal disease, as defined in the introductory portion of the Materials and Methods, Clinical section, as recorded in Table I. Even though there were marked differences in severity among family mem-

bers, those who required keratoplasty had very symmetrical posterior corneal and iris findings. Edema sometimes varied greatly between the two eyes, indicating endothelial decompensation and resulting in asymmetrical visual acuities. Nine (41%) transplants were performed on eyes having severe corneal disease. Thirteen (59%) had moderate disease.

The postoperative visual acuities following the 22 grafts at the time of the patient's last examination are shown in Table I. Eleven eyes (50%) had a visual acuity of 20/20 to 20/40, 1 eye (5%) was in the range of 20/50 to 20/100, 4 eyes (18%) were between 20/120 and 20/400, and 6 eyes (27%) had a visual acuity of worse than 20/400. Postoperative visual acuity was worse than that recorded preoperatively following three (14%) corneal transplants.

There are many reasons why eyes with clear corneal transplants can have poor vision. These include cystoid macular edema or other retinal pathology, cataracts, high refractive errors, and optic nerve disease. Only one of the ten eyes with 20/200 or less visual acuity had a clear graft (case 3). In that case, the poor vision was due to glaucomatous optic nerve damage. Nine eyes (41%) had 20/200 or less visual acuity because of cloudy corneas. The failed transplant was due to graft rejection in two eyes (22% of failed grafts, 9% of total grafts), glaucoma in three eyes (33% of failed grafts, 14% of total grafts), retrocorneal membrane in one eye (11% of failed grafts, 5% of total grafts), a combination of retrocorneal membrane and glaucoma in two eyes (22% of failed grafts, 9% of total grafts), and a combination of graft rejection and glaucoma in one eye (11% of failed grafts, 5% of total grafts).

Endothelial rejection reactions characterized by a typical endothelial rejection line or diffuse endothelial involvement with scattered keratic precipitates and anterior chamber inflammation were seen in seven patients (54%) and seven eyes (32%). Four of these patients (57%) were younger than 50 years of age. Of the seven eyes with corneal transplant allograft reactions, four (57%) responded favorably to corticosteroid therapy but only three ended up with 20/40 or better visual acuity. One (case 6) responded well but had poor visual results secondary to glaucoma. Three grafts failed because of graft rejection (43% of endothelial rejections, 14% of total grafts). It should be noted, however, that in one of these cases with graft failure due to rejection, poor compliance with medication instructions was a major problem.

Retrocorneal membranes were observed in four (18%) of the corneal grafts. In three of these four the transplanted corneas became cloudy (not case 3). All of the retrocorneal membranes formed in eyes that were noted to have slit lamp-visible iridocorneal adhesions preoperatively. In addition, these four eyes had postoperative glaucoma.

Thirteen of the 22 eyes (59%) undergoing penetrating keratoplasty for PPMD had iridocorneal adhesions preoperatively. Of these 13 eyes, 11 (50%) had adhesions which were visibly by slit lamp examination and 2 (9%) required gonioscopy. Four of the 13 eyes (31%) with iridocorneal adhesions ended up with 20/40 or better visual acuity. Nine eyes (69%) had a final visual acuity of 20/400 or worse. If the two cases of gonioscopic adhesions are excluded, the results change to only 2 of 11 eyes (18%) with visual acuities 20/40 or better and 9 of 11 (82%) with 20/400 or worse. Of the 11 of 22 eyes without slit lamp-visible iridocorneal adhesions, 9 had 20/40 or better visual acuity and 10 had clear grafts. One patient (case 11) had 20/80 visual acuity with a cataract and the other (case 7), believed not to be compliant with medicine instructions, failed from graft rejection and had a visual acuity of 20/200. Of nine eyes without iridocorneal adhesions (either slit lamp-visible or gonioscopic), seven (78%) had 20/40 or better visual acuity, one (11%) had 20/80, and one (11%) had 20/400 visual acuity.

Preoperative glaucoma, as defined as intraocular pressure greater than 20 mm Hg, was present in eight patients (62%) and in 13 eyes (59%). All eyes with preoperative glaucoma had iridocorneal adhesions. No corneal transplants were performed on eyes that did not have adequate control of intraocular pressure at the time of surgery.

Postoperative glaucoma was present in all of the eyes that had preoperative glaucoma. Four of these eyes (31%) required cyclocryotherapy at some time after their corneal transplant (case 6 OD, case 8 OD, case 9 OU). One eye underwent trabeculectomy at the time of penetrating keratoplasty (case 9 OS). Two eyes (15%) required a filtering procedure at some time after their corneal transplant (case 8 OD and case 9 OS). Case 6 had a trabeculectomy OD prior to keratoplasty. No elevated intraocular pressure problems were encountered in patients who were free of preoperative glaucoma and iridocorneal adhesions. Of the 13 corneal transplants done on eyes with glaucoma, 9 (69%) have resulted in a final visual acuity of 20/400 or less.

DISCUSSION

After having the opportunity to examine a large number of patients (approximately 120) with posterior polymorphous dystrophy, I can make several general points concerning their findings. Slit lamp examination of these patients revealed a spectrum of clinical findings, including the following: (1) Corneal edema which can vary from no edema, minimal stromal edema without epithelial edema, diffuse stromal edema with

epithelial haze or microcystic edema, to bullous keratopathy. (2) Calcific and lipid degenerative changes in severe cases. (3) Thickening of Descemet's membrane which may appear as excrescences projecting into the anterior chamber or as white patches that may be isolated or involve the entire posterior corneal surface. In retroillumination the thickened Descemet's membrane has a peau d'orange texture. (4) Band-like lesions at the level of Descemet's membrane with edges that are scalloped, irregular, and not parallel. (5) Posterior corneal vesicles in either a coalescent form, or isolated lesions, usually without corneal edema. (6) Islands of abnormal cells surrounded by normal-appearing endothelial cells. (7) Iridocorneal adhesions which varied from fine or broad-based adhesions seen only by gonioscopy, to large adhesions sometimes attached to the cornea by a glass-like membrane and seen easily by slit lamp examination. Several of these eyes had pupillary ectropion and corectopia.

Although most patients did not have elevated intraocular pressures, about 14% of the skewed population that I examined did. Most patients with elevated pressure had iridocorneal adhesions. Glaucoma in patients with slit lamp-visible broad-based adhesions, especially those with glass-like membranes, became more difficult to manage after corneal transplant surgery.

Thirteen of the approximately 120 patients required penetrating keratoplasty because of decompensation of one or both corneas with the development of stromal and epithelial edema. Many of the younger affected patients will no doubt someday need surgery. This is not to imply that at a given time one should expect that approximately 10% of eyes with posterior polymorphous dystrophy will require a cornea transplant. At our institution we see a patient population that is skewed toward substantially more corneal involvement and therefore the true incidence of corneal decompensation is much smaller. Most cases of posterior polymorphous dystrophy do not require treatment and involve asymptomatic posterior corneal lesions.

The literature contains several cases of patients requiring penetrating keratoplasty for posterior polymorphous dystrophy. These reports concentrate on the histopathologic findings of the corneal buttons and not on the postoperative course. To define the visual prognosis and incidence of complications after keratoplasty for posterior polymorphous dystrophy, we conducted a retrospective analysis of 22 consecutive corneal transplants done on 20 eyes of 13 patients with this disorder.

If one defines successful corneal transplant surgery as a postoperative visual acuity of 20/40 or better, we achieved a success rate of 50% (11 of 22 transplants). If success is measured by a clear corneal graft, our success

rate was 55% (12 of 22 transplants). Three complications were responsible for the failures in this series. These were: endothelial rejection, glaucoma, and retrocorneal membranes.

Endothelial rejection reactions were seen in seven patients (54%) and seven eyes (32%). Of the seven patients less than 50 years old, four (57%) were observed to have an endothelial rejection. We have previously reported[21] the incidence of endothelial graft rejection reaction in 156 penetrating keratoplasties performed for a variety of diseases to be 21%, with a higher incidence in vascularized corneas and in patients younger than 50 (32%). An extensive analysis has recently been reported by Arentsen[22] in which he studied factors that influence the rate of allograft reaction. He did not find a statistically higher incidence in younger patients. The number of patients and graft rejections in the present series is too small to provide statistically meaningful data. Two corneal grafts (9%) failed because of graft rejection alone and one (5%) failed due to a combination of rejection and glaucoma.

There are two forms of glaucoma which have been documented in patients with posterior polymorphous dystrophy. One type involves open angles. The exact mechanism in these cases has not been fully elucidated. It has been postulated[23] that a high iris insertion leads to collapse of the trabecular meshwork resulting in increased resistance to aqueous outflow. The second clinical form of glaucoma involves angle closure with extensive iridocorneal adhesions. Histologic study[14] has revealed a membrane consisting of epithelial-like endothelial cells extending down from the cornea across the chamber angle and onto the surface of the iris.

In this series, eight patients (62%) and 13 eyes (59%) had preoperative glaucoma. The exact incidence of glaucoma in posterior polymorphous dystrophy is not known. However, in our previous report[5] on the clinical spectrum of posterior polymorphous dystrophy, 8 (14%) of 59 patients with this dystrophy had elevated intraocular pressure. It can be postulated that a compromised but adequately functioning endothelium is further damaged by elevated intraocular pressure, and thus these corneas are likely to decompensate and develop stromal and epithelial edema necessitating a cornea transplant. This would explain why such a large number (62%) of our patients requiring penetrating keratoplasty had glaucoma. Another reason for a higher incidence of decompensated corneas in patients with glaucoma is that with glaucoma, especially when the glaucoma is due to epithelial-like cells growing over the trabecular meshwork, tend to have more severe corneal disease.

All eyes with preoperative glaucoma continued to have elevated intraocular pressure after penetrating keratoplasty. The final visual outcome

for these eyes was distinctly different than that for eyes without glaucoma. Sixty-nine percent of eyes with glaucoma had a final visual acuity of 20/400 or less. No normotensive eyes had a final visual acuity of 20/400 or less. We found this form of glaucoma to be extremely difficult to manage. Carbonic anhydrase inhibitors, filtering procedures, and cyclocryotherapy were used but not found to be as effective as in other cases of postkeratoplasty glaucoma.[24,25] Patients with broad-based iridocorneal adhesions are at a high risk of requiring future filtering procedures. Therefore, I would recommend extracapsular extraction if a cataract procedure is necessary.

Iridocorneal adhesions are now a well-recognized part of the spectrum of PPMD.[1,5,26] In the present series, 62% of the patients had iridocorneal adhesions. This compares with 16 of 59 patients (27%) with iridocorneal adhesions that we reported previously.[5] Perhaps the presence of iridocorneal adhesions is associated with a poorer functioning posterior layer of the cornea and thus a higher incidence of corneal decompensation. Alternatively, it may be the glaucoma that is associated with iridocorneal adhesions that causes these corneas to fail as explained above, or possibly a combination of both of these mechanisms. It is obvious that eyes with iridocorneal adhesions had a much lower success rate (31% resulting in 20/40 or better visual acuity) when compared to eyes without iridocorneal adhesions (78%). Those with adhesions easily visible by slit lamp examination had an even lower (18%) success rate. Thus, it seems that the presence of broad-based iridocorneal adhesions, especially if visible without gonioscopy, was the factor with the greatest influence on surgical outcome.

The occurrence of retrocorneal membranes in this series of patients was puzzling. If the leading edge of the membrane is thickened, it can be confused with an endothelial rejection line. It was not until our most recent patient with a retrocorneal membrane (case 6) that we suspected that it might be due to the recurrence and growth of a sheet of epithelial-like endothelial cells in the form of a membrane. Laboratory investigation has disclosed such an epithelial-like cell membrane from her previously failed donor button. We are currently completing this study and it will be the subject of a future report.

Severe corneal disease, as defined in the introduction to the Materials and Methods, Clinical section, did not correlate with iridocorneal adhesions. From careful observations recorded in the records of our institution, and from our own personal examinations, the corneal and iris findings prior to any operation on the 26 eyes of these 13 patients can be stated. Of the 26 eyes, 10 (38%) had severe corneal disease. Six of the 10

(60%) had adhesions and 4 (40%) did not. Of the 26 eyes, 16 (62%) had moderate corneal disease. Ten of the 16 (63%) had adhesions and 6 (37%) did not. The chances for a clear graft did not depend on the severity of preoperative corneal disease. Interestingly, of the 9 eyes with severe disease, 6 (67%) ended with clear grafts, and of the 13 with moderate disease, 7 (53%) had clear grafts.

Laboratory findings in posterior polymorphous dystrophy will be summarized in their chronologic order of publication. These observations will then be discussed, comparing them to our work.

The first histopathologic description of PPMD was published by Morgan and Patterson[7] in 1967. The keratoplasty specimen from this sporadic case revealed vacuoles and fusiform excrescences in Descemet's membrane similar to Hassall-Henle warts. The endothelium appeared to be normal except for areas of thinning related to the excrescences. Hogan and Bietti[27] studied a case of "hereditary" deep dystrophy of the cornea histochemically and by light and electron microscopy. This is the only reported case of PPMD in which calcium crystals were identified within deep corneal lamellae. Diffuse thickening of Descemet's membrane and cornea guttata were observed. The corneal endothelium was either absent or very thin. Boruchoff and Kuwabara[8] were the first to accurately describe the ultrastructural appearance of Descemet's membrane and the corneal endothelium. They found that the fine structural appearance of the anterior portion of Descemet's membrane was normal, but that the posterior portion consisted of abnormal collagen fibers and basal lamina substance. They thought the corneal endothelium had been replaced or transformed into epithelial cells since the cells possessed prominent microvilli, abundant keratofibrils, desmosomes, and sparse microorganelles. Independently, Hanselmayer[28,29] described by light and by electron microscopy irregularities and splitting of Descemet's membrane. The few remaining endothelial cells from the single keratoplasty specimen showed signs of "transformation and degeneration." Fusiform swellings and areas of cavities in Descemet's membrane were found by Malbran.[30]

Grayson[1] performed scanning and transmission electron microscopy on two corneal buttons of brothers and posterior polymorphous dystrophy. He confirmed the findings of earlier studies and speculated that metaplasia of the corneal endothelium could account for the peculiar appearance of the cells lining the posterior cornea. Tripathi et al[31] reported results similar to those of Bouchoff and Kuwabara[8] regarding epithelial-like cells in PPMD. They also found degenerating endothelial cells containing flocculent material. Another report[32] of epithelial-like endothelial cells in PPMD also pointed out that the corneal condition can be congenital and

therefore should be in the differential diagnosis of a case of congenital cloudy cornea. Hanna et al[33] reported a thin rather than thick Descemet's membrane in a 15-year-old who underwent penetrating keratoplasty and felt that its size was related to the patient's age. Johnson and Brown[34] found fusiform nodular Descemet's protrusions. Nodular thickening of Descemet's was also reported by Liakos and Casey.[35]

In 1980, we reported[14] the histopathology of the trabecular meshwork and iris in a case of PPMD. Epithelial-like endothelial cells were found growing down from the cornea across the trabecular meshwork and onto the iris. That year, we further characterized[17] these cells as epithelial cells by demonstrating keratin staining.

Polack and co-workers[36] stressed the finding of pits in an 8-year-old who underwent penetraing keratoplasty. Witschel et al[37] reported a family with peripheral corneal PPMD characterized by epithelial-like cells reaching into the periphery. Descemet's membrane became thinned and then absent peripherally. Waring[38] described a fibrocellular posterior collagen layer produced by fibroblasts possibly originating from transformed endothelial cells. Cibis and Tripathi[39] found the pathology of band formation in PPMD to be a thickening of Descemet's membrane covered by attenuated, degenerated endothelial cells. Hirst and Waring[40] used specular microscopy to demonstrate vesicular lesions surrounded by large pleomorphic cells and geographic lesions surrounded by smaller cells. Bourgeois et al[23] demonstrated histopathologically that glaucoma need not be caused by a membrane of epithelial-like endothelial cells growing down over the trabecular meshwork in PPMD. They reported a case of glaucoma and PPMD where there was an anterior insertion of the iris into the trabecular meshwork without the extra membrane.

An excellent review of the histopathology of PPMD and a report of nine corneas from patients with the condition was recently published by Henriquez and co-workers.[41] They emphasized endothelial cell degeneration and loss and what they considered to be fibroblastic and epithelial-like cell transformation. They felt that the Descemet's changes, including lamination, deposition of abnormal collagen, pits, and guttate excrescences, were secondary.

The histologic findings in posterior polymorphous dystrophy described by the above mentioned investigators have been confirmed by our work.[19,20] Descemet's changes, which we also believe are secondary to endothelial pathology, include a multilaminar structure, guttate excrescences, collagen fibril deposition, fiberoptic cell presence, normal anterior banding with pathologic posterior banding, thick areas, thin areas, and all thicknesses in between, and extra basement membrane material.

TABLE II: MORPHOLOGIC AND GROWTH FEATURES IN COMMON BETWEEN NORMAL EPITHELIAL CELLS AND PPMD ENDOTHELIAL CELLS

1. Multilaminar pattern
2. Desmosomal junctions
3. Microvillous projections
4. Cytoplasmic keratin
5. Sparse mitochondria
6. Rapid growth in tissue culture

Our studies have disclosed all of the cell types lining the posterior cornea that others have described, including rather normal appearing endothelial cells, attenuated, degenerating, vacuolated endothelial cells, fibroblast-like cells, and, most characteristically, epithelial-like cells. Table II summarizes features that these cells have in common with normal epithelial cells.

Certainly the presence of degenerated, vacuolated, attenuated large pleomorphic endothelial cells play an important role in endothelial decompensation and subsequent stromal and epithelial edema. It is not certain what factor epithelial-like cells contribute to the edema. When edema is sufficient to significantly reduce vision, patients usually require penetrating keratoplasty. If these epithelial-like cells have not already grown across the trabecular meshwork and onto the iris to cause glaucoma and broad-based anterior synechiae, the prognosis for keratoplasty is excellent. Cell culture studies demonstrate rapid growth of these cells that have morphologic similarities to epithelial cells. Laboratory studies made us aware of the aggressiveness of these cells, and we, therefore, had a better idea of what would happen postoperatively in patients who preoperatively showed broad-based synechiae and had glaucoma. Case 6 exhibited a regrowth of these epithelial-like cells onto the posterior surface of the donor graft. Some of the retrocorneal membranes that were seen clinically might be other examples of this aggressive cell type. It is possible that even some patients in whom we felt a graft rejection was taking place might have, instead, been experiencing spread of epithelial-like cells.

What is the origin of the epithelial-like cells in PPMD? Most authors who have published reports concerning PPMD have tried to answer that question, yet no one is certain of their origin. Since posterior polymorphous dystrophy may be congenital, the cells probably date their existence in some cases to before birth. Three possibilities seem apparent. First, they could represent cell rests. Second, the cell line which nor-

mally produces endothelial cells could have produced epithelial cells instead. Or third, they might have first been endothelial cells which transformed for an unknown reason into epithelial-like cells. Perhaps this question will someday be answered when we know more about embryonic development of the cornea.

Clinical and laboratory experience over the past 10 years have led me to the following conclusions concerning this interesting corneal condition. Some of these conclusions are firmly based on factual evidence; others are merely personal opinion.

1. Posterior polymorphous corneal dystrophy is an autosomal dominantly inherited disease. Rare examples of affected siblings with unaffected parents may suggest another form of inheritance, but these cases can also be explained by low penetrance.

2. Posterior polymorphous corneal dystrophy is almost always a bilateral condition. There are rare cases of unilateral involvement within families where other members have the classic condition. Unilateral posterior corneal vesicular-appearing lesions occur in patients whose families are not affected.[42] Because such patients have a unilateral condition with a negative family examination, I am unable to call their condition a "dystrophy," but think of it more as an isolated physical finding.

3. I do not consider posterior polymorphous dystrophy to be part of a spectrum that includes Fuchs' dystrophy and congenital hereditary endothelial dystrophy (CHED). The clinical findings and pathology of Fuchs' dystrophy and CHED are considerably different from PPMD. It is true that all three are endothelial dystrophies, but I see no reason to lump them together.

4. The incidence of PPMD, although not statistically defined, is no doubt greater than most would expect. Some may be unrecognized in the clinic. Even after years of experience with PPMD patients, I have been unsure of the diagnosis on initial examination (cases 12 and 13). And, since many patients (possibly the majority) are asymptomatic, PPMD can occur in the general population undiagnosed.

5. The spectrum of corneal findings in PPMD ranges from a few vesicular-appearing lesions to total cloudiness of the cornea with edema and calcific and lipid degeneration. The iris can be uninvolved, exhibit peripheral anterior synechiae seen only on gonioscopy, or be peripherally adherent in broad bands to the cornea and seen easily by slit lamp examination.

6. Glaucoma, although present in only a minority of patients with PPMD, is a frequent problem in symptomatic patients. It is often extremely difficult to manage, especially after a corneal transplant.

7. Although four types of cells covering the posterior surface of the cornea are seen in the laboratory ("normal" endothelial cells, attenuated and degenerated cells, fibroblast-like cells, epithelial-like cells), it is the epithelial-like cells that so strongly influence the success or failure of a keratoplasty and the incidence and severity of the glaucoma.

8. Penetrating keratoplasty for PPMD has an excellent prognosis if glaucoma and/or iris adhesions are not present preoperatively. If they are present, although there are exceptions, the prognosis is usually poor. I would try to avoid operating on a patient with slit lamp-visible broad-based iridocorneal adhesions if at all possible. Iridocorneal adhesions influence the prognosis of a keratoplasty more than the severity of the corneal disease.

Many workers throughout the world are continuing to investigate this disease. The epithelial-like cell membrane that can grow across the trabecular meshwork onto the iris and can regrow after an operation, more than any other factor, determines the prognosis for glaucoma control and corneal transplant success. Future laboratory findings may give us clues concerning the nature and management of this tissue.

SUMMARY

This thesis contains a clinical and laboratory summary of findings in PPMD and, for the first time, reports the results of a large series of patients who underwent keratoplasty surgery. Posterior polymorphous dystrophy is bilateral and autosomal dominantly inherited. Slit lamp findings include corneal edema in the more advanced cases, calcific and lipid degenerative changes in severe cases, band-like lesions at the level of Descemet's membrane, localized or diffuse thickenings of Descemet's membrane, posterior corneal vesicular-like lesions, islands of abnormal cells surrounded by normal-appearing endothelial cells. Iridocorneal adhesions ranged in severity from fine or broad-based adhesions seen only on gonioscopy to large iridocorneal adhesions often associated with a glass-like membrane that are seen easily by slit lamp examination. All patients with broad-based iridocorneal adhesions have elevated intraocular pressure. Some patients have elevated pressure but no adhesions.

Laboratory examination of corneal, iris, and trabecular meshwork tissue from patients undergoing penetrating keratoplasty and filtering operations reveals an abnormal endothelial cell layer covering the posterior cornea and growing across the trabecular meshwork and onto the iris. Although this tissue contains a variety of cells, the most prominent type is an epithelial-like cell. Extensive laboratory studies demonstrate features

in common between the epithelial-like cells and normal epithelium. These include a multilaminar pattern, desmosomal junctions, microvillous projections, cytoplasmic keratin, sparse mitochondria, and rapid growth in tissue culture. These cells appear to determine the management and prognosis of patients with PPMD undergoing surgery.

Twenty-two corneal transplants were performed on 20 eyes of 13 patients with PPMD. Their ages ranged from 11 to 77 years. The follow-up time after keratoplasty averaged 4.75 years.

Nine grafts (41%) failed. Two failed because of an endothelial rejection, three because of glaucoma, one because of a retrocorneal membrane, two from both a retrocorneal membrane and glaucoma, and one from both an endothelial rejection and glaucoma. Thus, glaucoma was involved in six of the nine failures (27% of all grafts). Clinically visible retrocorneal membranes formed in 4 of the 22 grafts. All four eyes had preoperative slit lamp-visible iridocorneal adhesions. The factor that most prominently influences keratoplasty prognosis is the presence of iridocorneal adhesions. When the adhesions were visible without gonioscopy, 82% had 20/400 or worse visual acuity. On the other hand, when either no adhesions were seen or adhesions were only seen by gonioscopy, 91% had a clear corneal transplant and 82% had a visual acuity of 20/40 or better. One patient had a visual acuity of 20/80 with a cataract and another patient had a failed graft due to endothelial rejection with a visual acuity of 20/200. Every case with iridocorneal adhesions had both preoperative and postoperative glaucoma. The severity of corneal disease did not correlate with the chance of a clear corneal transplant.

Because of the very poor chance of a clear corneal transplant and the high likelihood of severe glaucoma problems, PPMD patients with slit lamp-visible iridocorneal adhesions should not undergo keratoplasty until absolutely necessary. On the other hand, if that type of iridocorneal adhesion does not exist, the prognosis for a good outcome is excellent.

ACKNOWLEDGMENTS

I gratefully acknowledge Drs Frederick C. Blodi and Robert C. Watzke for sponsoring me and guiding me through the preparation of this manuscript. Drs Charles D. Phelps and H. Stanley Thompson also provided advice in its preparation. I thank my teacher, Dr Peter R. Laibson for his encouragement not only regarding this endeavor but throughout my career. Over the years, my research regarding PPMD represents the collaborative efforts of Drs Gerhard W. Cibis, Charles D. Phelps, Thomas A. Weingeist, David A. Newsome, Tung-Tien Sun, and in particular,

Merlyn M. Rodrigues. I hope that I have represented our data accurately and that they will forgive me if opinions I have expressed differ from theirs. Robert B. Taylor was responsible for sectioning, preparing, and shipping tissue to the National Eye Institute and other collaborating locations. Patricia J. Mason provided editorial assistance. Sandra A. O'Neill typed all drafts and the final manuscript. I especially want to thank my present cornea fellow, Dr Michael B. Shapiro, for encouraging and helping his teacher to report our experience with PPMD.

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